7 June 2011

YM BioSciences

Year end	Revenue (C$m)	PBT* (C$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/09	4.5	(11.6)	(20.1)	0.0	N/A	N/A
06/10	2.6	(17.3)	(26.8)	0.0	N/A	N/A
06/11e	1.2	(22.9)	(24.0)	0.0	N/A	N/A
06/12e	0.9	(22.0)	(18.3)	0.0	N/A	N/A

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

Investment summary: JAK in the box

The oral JAK1/2 inhibitor CYT387 has emerged as YM BioSciences' lead development project, having been acquired through last year's takeover of the Australian biotech company Cytopia. YM's investment case centres on progressing CYT387 through development, thus derisking the project, and signing future licensing deal(s). Further Phase I/II data have been presented at ASCO, and YM's hand in negotiations has been strengthened by a recent fund-raising.

Big pharma interest in JAK

Three significant deals involving competing JAK inhibitors have been struck in the past 18 months or so – showing big pharma's growing interest in the JAK inhibitor mechanism – and CYT387 is one of the most advanced unpartnered projects in development. It is also the only one to have shown a significant response rate in anaemia in myelofibrosis, which could help to differentiate it from competitors.

ASCO presentations underscore potential

YM has reported further interim Phase I/II data for CYT387 at the ASCO meeting, confirming the project's positive effect on anaemia, in addition to benefits in spleen volumes and constitutional symptoms. Full study readout, expected by the end of 2011, could derisk the project further and crystallise more value for YM.

Key competitor filed

The most advanced JAK inhibitor, Novartis/Incyte's ruxolitinib, has just been filed for US approval; if launched this will set the market for CYT387, which has shown added benefits. YM is one of the better-financed biotech companies of its size, with sufficient cash to last well beyond FY12, even in the absence of new deals.

Valuation: Anaemia benefit gives upside

A mid-case view of CYT387's potential market share appears to support YM's current market cap, but a key factor will be the agent's anaemia effect. If this benefit results in a 50% market share, for instance, the valuation becomes C$474m. The $500m to $1bn 'biodollar' value of JAK inhibitor deals could justify a further premium.

Price	C$3.30
Market cap	C$386m

Share price graph

Share details

Code	YMI.US, YM.TO
Listing	Amex, TSX
Sector	Pharmaceuticals & Biotechnology
Shares in issue	117m

Price

52-week	High	Low
	C$3.47	C$1.06

Balance sheet as at 31 March 2011

Debt/equity (%)	N/A
NAV per share (c)	67
Net cash (C$m)	73.5

Business

YM BioSciences is an oncology-focused business developing compounds licensed from academia and acquired through takeovers. Its stock is listed on Amex and the Toronto Stock Exchange.

Valuation

	2010	2011e	2012e
P/E relative	N/A	N/A	N/A
P/CF	N/A	N/A	N/A
EV/sales	N/A	N/A	N/A
ROE	N/A	N/A	N/A

Revenues by geography

UK	Europe	US	Other
0%	0%	0%	100%

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Investment summary: Canadian cancer drug developer

Company description

YM BioSciences is a Canadian drug development company focused on oncology. It is dual-listed on NYSE Amex and the Toronto Stock Exchange, having delisted from AIM in October 2009. In February 2010, YM completed the acquisition of Cytopia, an Australian biotech firm, issuing 7.2m new shares (~C$13m) as consideration for all issued and outstanding Cytopia shares. Through Cytopia, YM gained what is now its lead project, CYT387. Previous acquisitions include Eximias Pharmaceutical in 2006 and Delex Therapeutics in 2005.

Exhibit 1: YM BioSciences' R&D pipeline summary

Product	Stage	Indications/notes
CYT387	Phase I/II	Myeloproliferative disorders.
Nimotuzumab	Phase III	Multiple cancers. Sub-licensed to Daiichi Sankyo, Oncoscience and others.
CYT997	Phase II	Glioblastoma multiforme, multiple myeloma.

Source: Edison Investment Research

Valuation: Anaemia benefit gives upside

CYT387 is now the major input in the valuation model for YM, and we assume a current potential market worth $500-750m for its first indication, myelofibrosis. Other myeloproliferative neoplasms represent indications that could take the potential market to $2bn and beyond. The possible share that CYT387 could seize is an important valuation input, and a mid-case view (37.5% share with standard risk adjustments) appears to support YM's current market cap. However, a key benefit will be the anaemia effect demonstrated by CYT387, and this might take the share up to 50%, yielding an indicative valuation of C$474m. As CYT387 advances through development, added value will be crystallised, and recent JAK inhibitor licensing deals could justify a further premium.

Sensitivities

The potential market size for myelofibrosis and other myeloproliferative neoplasms will depend on YM BioSciences' and other companies' ability to charge premium prices, and the share of this market that CYT387 can seize is a key variable in our valuation methodology for YM. As no up-front or milestone payments on potential future deals are factored into our model, these represent potential upside to our assumptions. In addition to typical biotech company risks, the US economic embargo on trade with Cuba is the most important sensitivity regarding nimotuzumab's approval/licensing in the US. It is also possible that the perceived complexity of the nimotuzumab consortium might deter licensees and acquirers (other than Daiichi Sankyo).

Financials

YM reported a balance of cash and equivalents of C$73.5m at its fiscal third-quarter end (31 March 2011), largely thanks to a fund-raising in December that brought in net proceeds of C$43.3m, including the exercise of an over-allotment option. The exercise of certain options and warrants raised a further C$1.8m in the nine-month period. Thanks to the issue during the fiscal fourth quarter of 5.2m out of a possible 7.8m shares under a recent controlled equity offering, we expect YM to finish the current fiscal year with cash of C$74m; our model shows the company to be financed well beyond fiscal 2012, even if higher R&D, and general and administrative spending as a result of the Cytopia takeover, are factored in.

Investment summary: JAK in the box

YM BioSciences is an oncology-focused biotechnology company based in Ontario, Canada, with stock listed on NYSE Amex and the Toronto Stock Exchange. It is developing a small pipeline of mid-stage projects for a wide range of cancer indications, and in February 2010 completed the acquisition of the Australian biopharmaceutical company Cytopia.

The acquisition of Cytopia broadened YM's development portfolio, adding two early-stage oncology assets, CYT387 and CYT997, the former of which is now YM's lead development project. While CYT387 is now the lead, development of nimotuzumab, a potential best-in-class cancer monoclonal antibody originated by Cuba's Centre of Molecular Immunology, is increasingly in the hands of a consortium of partners and licensees, with YM providing a supporting role.

YM remains relatively well financed, with cash of C$73.5m at its fiscal third-quarter end (31 March 2011), largely thanks to a fund-raising completed in December that brought in net proceeds of C$43.3m. The group's investment case centres on continued development of the lead projects, with reporting of data for key clinical trials – such as interim data of the Phase I/II study of CYT387 just presented at ASCO, and full data readout expected at the ASH conference in late 2011 – possibly leading to partnering activity.

The combined R&D portfolio following the Cytopia acquistion is summarised below in Exhibit 2.

Exhibit 2: YM BioSciences' R&D pipeline

Product	Indication	Development stage/notes
CYT387	Myeloproliferative disorders (Phase I/II)	Oral JAK1/2 inhibitor. 155-pt Phase I/II study in myelofibrosis. Interim safety, tolerability and efficacy data from first 60 pts presented at ASCO 2011, showing positive effect on anaemia, a major life-shortening symptom associated with myelofibrosis (in addition to reducing spleen volumes and improving constitutional symptoms). Advanced data is expected late 2011. Phase III studies possible in H112. Potential use in polycythemia vera, essential thrombocythemia and other oncology indications. Follow-up compounds could target inflammatory use, such as RA. Composition-of-matter patent to 2027, plus extensions. US orphan drug status, and positive COMP opinion on EU orphan drug status.
Nimotuzumab	Paediatric diffuse pontine glioma, adult glioma, squamous head and neck cancer (Phase III)/ pancreatic cancer, NSCLC, NSCLC brain metastases, gastric cancer and cervical cancer (Phase II)	Humanised MAb targeting EGFR. Phase II and III studies under way in multiple cancer types. YM licensed developed world rights from CIMAB (via YM subsidiary, CIMYM) and sub-licensed rights to **Daiichi Sankyo** in Japan, **Oncoscience** in Europe, **Innogene Kalbiotech** (minor countries in Africa and Asia) and **Kuhnil** (South Korea). CIMAB has independently licensed a number of other companies in the developing world. Marketed by several companies in secondary markets for glioma and head and neck cancer. EU submission (by Oncoscience) possible in 2011. Phase III studies under way in adult glioma (Oncoscience: data H1 2011) and squamous cell carcinoma of the head and neck (National Cancer Center of Singapore/Innogene Kalbiotech). Results of Daiichi Sankyo Phase II trial (first-line NSCLC) expected in H1 2011, and should confirm a Phase III decision in 2011. Recruitment into YM's two randomized Phase II clinical trials of nimotuzumab in NSCLC proved slower than had been expected, and the studies have been stopped.
CYT997	Glioblastoma multiforme (Phase Ib/II)/multiple myeloma (Phase II)	Vascular disrupting agent (potential for oral and iv admin). 35-pt Phase Ib/II single arm iv study in relapsed GBM + carboplatin and etoposide (Ph I results 2010/Ph II: H211). 24-pt Phase II in relapsed/refractory multiple myeloma has been terminated after difficulties recruiting patients. Phase I iv and oral results at ASCO 2008 and 2009 (good tolerability and efficacy signals). Full Phase I iv results published in the British Journal of Cancer (2010) 103, 597-606. Oral formulation undergoing product formulation and preclinical development.
Focal adhesion kinase (FAK)	Solid tumours (preclinical)	Collaborative research project with Cooperative Research Centre for Cancer Therapeutics in Melbourne. FAK is linked to cancer cell migration, proliferation and survival.
Small molecules	PAH (preclinical)	Licensee Pulmokine is developing novel therapies which inhibit development and progression of pulmonary arterial hypertension (PAH). NIH research grants awarded for Phase I trials.
Nimotuzumab indium-111	Solid tumours (discovery)	Radiolabelled version of nimotuzumab.
Anti-HER2 conjugate	Breast cancer (discovery)	Discovery programme to develop conjugated, rationally designed selective anti-HER2/neu monoclonal antibody (that does not target HER2 on cardiac cells).

Source: Edison Investment Research

CYT387: New lead project

Following YM's takeover of Cytopia in February 2010, the company designated the novel orally active JAK1/JAK2-inhibitor CYT387 its new lead project in place of nimotuzumab (which remains an important YM project and is being studied in a number of clinical trials for a range of cancer indications).

CYT387 is being studied for treating myeloproliferative neoplasms, a use in which the JAK (Janus-activated kinase) mechanism is known to play a key role. JAK inhibitors are also implicated in the proliferation of various types of solid cancer (prostate, breast, head and neck, lung, ovarian, renal cell, glioma, pancreatic, liver) as well as in multiple myeloma, lymphoma and leukaemia. There are a number of competing JAK projects in development, and the most advanced – Novartis/Incyte's ruxolitinib – has just been filed for US approval (see Exhibit 3).

Exhibit 3: JAK inhibitors in clinical development for cancer and cancer-related indications

Name	Company	Mechanism	Notes
Ruxolitinib (INC424/ INCB18424)	Incyte (US)/ Novartis (ex-US)	JAK1/2 inhibitor	Filed for US approval 6 June 2011 on the strength of two studies in primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis: 309-pt US 24-week COMFORT-I (35% reduction in spleen volume seen in 41.9% of patients vs 0.7% for placebo (p<0.0001) and met secondary endpoint of symptomatic improvement) and 219-pt COMFORT-II (28.5% of patients achieved a reduction in spleen volume of 35% or more vs 0% of placebo recipients; p<0.0001). 300-pt Phase III RESPONSE trial in polycythemia vera ongoing, and Phase III in psoriasis expected to start imminently. US and EU orphan drug status.
Lestaurtinib (CEP-701)	Cephalon	Inhibitor of Flt3, TrkA & JAK2	Phase III: 224-pt trial in relapsed AML expressing Flt3-activating mutations (results: June 2012). In a 224-pt Phase II trial in the same pt population, pts on lestaurtinib + standard induction chemo showed no increased survival benefit.
AT9283	Astex Therapeutics	Aurora kinase/ JAK2 inhibitor	Phase II: 30-pt Phase II in relapsed/refractory multiple myeloma (results: June 2013), planned.
SB1518/ SB1578	S*BIO	JAK2 inhibitor	Handed back by licensee Onyx 4 May 2011. Phase II: first 10 pts enrolled into an open-label study in 87 pts with advanced lymphoid malignancies, to evaluate efficacy and safety. 400mg dosed orally; secondary endpoints include duration of response and progression-free survival. US orphan drug status for myeloproliferative disorders. Two Phase I/II trials: 49-pt chronic idiopathic myelofibrosis and 30-pt advanced myeloid malignancies (promising efficacy and good tolerability). 30-pt Phase I advanced lymphoid malignancies showed good tolerability. Presentation at ASCO 2011 confirmed durable responses in spleen volume reduction and symptom relief, especially in patients with impaired haematopoiesis. SB1578 is in a Phase I study in 64 volunteers.
CYT387	YM BioSciences	JAK1/2 inhibitor	Phase I/II: 140-pt Phase I/II myelofibrosis study ongoing. Recruitment target exceeded, with 155 pts recruited as of June 2011. Full data expected in H2 2011; pivotal Phase III studies possible Q1 2012. Orphan drug status.
AZD1480	AstraZeneca	JAK2 inhibitor	Phase I/II: 80-pt open-label US Phase I/II trial in primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis (results: Dec 2011).
SAR302503 (TG101348)	Sanofi-Aventis	JAK2 inhibitor	Phase I/II: Positive 60-pt Phase I/II trial in myeloproliferative neoplasms: results at ASH 2009. Obtained via TargeGen acquisition. Also targets Flt3 and Ret.
LY2784544	Lilly	JAK2 inhibitor	Phase I: 60-pt Phase I study in myeloproliferative disorders (results: Dec 2012).
SB1317	S*BIO/Tregara	JAK2 inhibitor	Phase I: Open-label study in 80 pts with advanced or refractory haematological malignancies (completion: Dec 2011).
AC430	Ambit	JAK2 inhibitor	Phase I: Placebo-controlled study in 88 volunteers. Completion: July 2011.
GLPG0634	Galapagos	JAK1 inhibitor	Phase I: 40-pt double-blind, placebo-controlled single and multiple ascending-dose study ongoing. 28-day, 36-pt Phase II study to start in 2011. Previously in development in a deal with GSK.

Source: Edison Investment Research

YM intends to begin discussions with the US FDA this year regarding the CYT387 Phase III programme and to focus on completing any remaining preclinical and manufacturing research needed before the project can enter a pivotal study, planned for H112. The company will also seek licensee(s) for the project.

Three significant deals involving competing JAK inhibitors have been struck in the past 18 months or so: Incyte licensed ex-US rights to ruxolitinib to Novartis in November 2009 for up to $1bn in milestones ($150m up front) and global rights to INCB28050 to Lilly in December 2009 for up to $755m in milestones ($90m up front); and Sanofi-Aventis acquired TargeGen in June 2010 for $560m ($75m up front) in a deal driven by the target's JAK2 inhibitor, TG101348. This indicates a growing awareness of, and interest in, the JAK inhibitor mechanism on the part of big pharma.

However, Onyx Pharmaceuticals recently handed back the rights to the JAK2 inhibitors SB1518 and SB1578 to originator S*BIO, terminating a licensing deal signed in January 2009.

Anaemia response a key differentiator

CYT387 is in a 155-patient, Phase I/II study for the treatment of myelofibrosis, a neoplasm in which excess cells are produced in the bone marrow, causing the bone marrow to be replaced by fibrotic scar tissue. Updated interim data on the anaemia response from this study were presented at the Florence Meeting on Myeloproliferative Neoplasms (16 April 2011) and ASCO (3 June 2011).

These confirmed the initial findings reported at ASH 2010 last December from 60 patients enrolled in the dose-escalation/confirmation part of the trial, of whom 33 were dependent on red cell transfusion. 19 of these 33 patients showed an anaemia response (defined as a ≥12-week transfusion-free period while on drug therapy with a haemoglobin level of ≥8g/dL), with a median duration of transfusion independence of six months (range: 4-15 months). Only two of these 19 patients subsequently required a single red cell transfusion.

The data reinforce the finding that CYT387 is so far the only JAK1/JAK2 inhibitor to have shown a significant response rate in anaemia in myelofibrosis, an important finding that could help to differentiate it from competitor products, especially as it is unlikely to be first to market. Anaemia is the most serious symptom in myeloproliferative neoplasms, and the response rate on anaemia could enable the product's eventual label to be extended into other indications where anaemia is a symptom. Data presented at ASH 2010 showed encouraging signs of efficacy, with an overall response rate of 62%.

The ASCO data showed a 92% retention rate after a median treatment duration of 6.4 months, and grade 3/4 haematological and non-haematological adverse events were infrequent except thrombocytopenia (in 25% of patients). Previously reported tolerability was good, with dose-limiting toxicities experienced by two of six patients at the highest (400mg/day) dose level.

Meanwhile, recruitment of the remaining 80 patients in the Phase II part of the trial has been exceeded, with 155 patients in total recruited as of June 2011. The release of full data is planned for late 2011, with a presentation scheduled at ASH in December.

Nimotuzumab: Largely reliant on licensees

Although the anti-EGFR monoclonal antibody nimotuzumab remains the most clinically advanced project in YM's pipeline, the company has de-emphasised its significance somewhat in favour of CYT387. However, nimotuzumab should continue to generate further clinical data, which could lead to additional licensing deals being signed, including possible sublicensing activity by YM's licensee Oncoscience. Another YM licensee, Daiichi Sankyo, might start a Phase III study in gastric cancer in 2012, subject to scale-up and manufacturing changes.

Nimotuzumab was originated by CIMAB, a Cuban biotech firm responsible for commercialising products discovered at Cuba's Centre of Molecular Immunology (CIM). It is currently being developed through a global consortium comprising a number of companies, many of which have a cooperative rather than a contractual relationship. The consortium allows members to opt in to the development of nimotuzumab in a given clinical study, which is sponsored by an individual member, but permits others to fund recruitment in their own territories (reducing cost to the sponsor) and share the data generated.

YM BioSciences (via its subsidiary CIMYM) licensed rights from CIMAB to develop nimotuzumab in the developing world, and subsequently sublicensed these rights to Daiichi Sankyo (for Japan), Oncoscience (Europe), Innogene Kalbiotech (Africa, Asia) and Kuhnil (South Korea). (Independently of this licensing/sublicensing arrangement, CIMAB has sublicensed rights to nimotuzumab in a number of developing-world markets.)

YM recently decided to end two Phase II studies in NSCLC owing to slow recruitment and their expected costs, and accordingly most of the value in the project resides in the direct licensing deals in which YM retains a late-stage interest. YM's own involvement is now limited to a Phase II study in paediatric progressive diffuse intrinsic pontine glioma, which has concluded recruitment and should report data in H211 (Exhibit 4).

Exhibit 4: Nimotuzumab studies under way (Phase II and above; YM and direct licensees only)

Indication	Sponsor	Status
Squamous head and neck cancer (adjuvant)	National Cancer Centre Singapore/ Innogene Kalbiotech	710-pt Phase III of cisplatin/radiotherapy ± nimotuzumab (400mg) (post-operative/adjuvant setting). Primary endpoint: DFS at two and five years. Secondary endpoints: OS at two and five years. Results: June 2012.
First-line pancreatic cancer	Oncoscience	188-pt Phase IIb/IIIa trial of gemcitabine ± nimotuzumab (400mg). Primary endpoint: TTP, OS; secondary endpoint: overall response.
First-line adult glioma	Oncoscience	148-pt Phase III study of temozolomide/radiotherapy ± nimotuzumab (150mg/m^2). Primary endpoint: PFS at six, 12 and 18 months. Updated data to be presented 2011 ASCO conference.
First-line non-NSCLC (curative intent, stage III)	Daiichi Sankyo	39-pt Phase II trial of RT/cisplatin/vinorelbine ± nimotuzumab (200mg). Primary endpoint is treatment completion rate and secondary endpoints include response rate, PFS, OS at 12 and 18 months and toxicity. Data to be presented H2 2011.
Cervical cancer	Innogene Kalbiotech	71-pt Phase II of nimotuzumab (200mg) + radiotherapy (ongoing).
Paediatric DIPG	YM BioSciences	44-pt Phase II single arm in recurrent disease (fully recruited). Results Q3 2011.
Paediatric diffuse intrinsic pontine glioma, first line	Oncoscience	42-pt Phase III study of nimotuzumab (150mg/m^2) + radiotherapy. Primary endpoint: PFS at six, 12 and 18 months. Pending EMEA approval of Paediatric Investigation Plan which would support marketing authorisation submission.
Squamous head and neck cancer	INCC Singapore Innogene Kalbiotech	37-pt Phase II of nimotuzumab (200mg) + cisplatin + radiotherapy in locally advanced disease (results: April 2010).

Source: Edison Investment Research

In addition to the above there are at least 15 clinical trials ongoing as part of licensing deals signed directly by CIMAB, including a 480-patient Chinese Phase III trial in nasopharyngeal cancer (Biotech Pharmaceutical) and a 104-patient Brazilian Phase II oesophageal cancer study (Eurofarma). However, as YM does not stand to receive any milestone or royalty income as part of these alliances, they are not considered in this note. Nimotuzumab is marketed by several companies in 24 countries including India, China, Argentina, Brazil and Mexico for glioma and head and neck cancer, and YM receives royalties from a limited European sales programme.

Some studies have suggested that nimotuzumab has comparable efficacy to currently marketed EGFR inhibitors such as the blockbuster Erbitux[1] (cetuximab, Bristol-Myers Squibb) and also Vectibix (panitumumab, Amgen), but with a much less toxic side-effect profile, in particular not giving rise to the severe skin and other toxicities typically seen with these agents. Presentations at the ASCO and AACR conferences in 2009 provided evidence that this profile was due to the drug's bivalent binding requirement, which also defines the cancer indications in which it is likely to be efficacious. These experiments demonstrated that, because of its confirmed monovalent binding, cetuximab binds indiscriminately to EGFR in healthy cells as in tumour cells. Nimotuzumab, unlike cetuximab, requires bivalency to bind cells, which results in the selective targeting of cells that over-express EGFR (eg carcinoma cells) and discriminates against healthy tissue, which expresses EGFR at lower densities. Nimotuzumab has been shown to be efficacious in cancers that naturally express high-density EGFR (eg glioblastoma, head and neck, gastric, cervical cancers), or any cancer treated with a radiation-containing regimen.

Exhibit 5 details Phase II studies with nimotuzumab that have been completed to date, again excluding those not carried out by YM or a direct licensee.

Exhibit 5: Completed nimotuzumab studies (Phase II and above; YM and direct licensees only)

Indication	Sponsor	Status
NSCLC (palliative), first line or later	YM BioSciences/ Kuhnil	128-pt Phase II of EBRT ± nimotuzumab (200mg) to treat intrathoracic disease from NSCLC pts diagnosed with Stage IIb or III NSCLC ineligible for curative treatment, or Stage IV NSCLC pts with progressive disease within the chest. Study closed owing to slow recruitment and cost issues.
Brain metastases from NSCLC, first line	YM BioSciences	88-pt Phase II of whole-brain radiation therapy WBRT ± nimotuzumab (200mg). Primary efficacy endpoint is the difference in intracranial disease progression over six months. Study closed owing to slow recruitment and cost issues.
Advanced or recurrent gastric cancer	Daiichi Sankyo/Kuhnil	80-pt Phase II open-label study irinotecan ± nimotuzumab in 5FU-refractory gastric cancer. Not powered for statistical significance, but subgroup analyses demonstrated that EGFR-positive patients treated with nimotuzumab showed a potential improvement of progression-free survival and overall survival
Advanced refractory pancreatic cancer	Oncoscience	65-pt Phase II completed of 100/200/400/800mg nimotuzumab. No data.
Irinotecan-refractory colorectal cancer	YM BioSciences	61-pt Phase II completed. 400mg. Study failed.
Paediatric diffuse intrinsic pontine glioma, first line	Oncoscience	47-pt Phase III study of nimotuzumab + radiotherapy. Primary endpoint: PFS at six, 12 and 18 months. Response to study treatment after 24 weeks was 75%. Median survival of all patients was recorded at 9.6 months (responders a median survival of 11.4 months). After one year 34% of patients were still alive (SIOP paediatric oncology forum October 2009). Preliminary data released at ASCO 2008.
Recurrent high-grade paediatric glioma	Oncoscience	34-pt Phase II study. Pts with glioblastoma multiforme, anaplastic astrocytoma or intrinsic pontine glioma (PG) with progressive disease following primary or relapse treatment. 12/34 pts showed response (PR, n=1, SD, n=11) in week-eight MRI, with clinical deterioration in four and markedly clinical improvement in two pts. Nine PR/SD were seen in the 14 pts with PG. 8 pts continued with the consolidation therapy. 5/8 pts were evaluable for response and showed three PR, one SD and one PD in week 21. Median PFS in these eight pts was 7.5 months (*J Clin Oncol*, 2006 Bode *et al*).

Source: Edison Investment Research

CYT997: Oral vascular disrupting agent

CYT997, a vascular disrupting agent (VDA), was acquired through Cytopia, whose in-house chemistry team had synthesised it. VDAs act by disrupting existing tumour blood vessels (in contrast to angiogenesis inhibitors such as Avastin (bevacizumab; Roche), which target novel blood vessel formation), and are believed to be applicable against a broad variety of tumour types –

[1] Reddy BK et al. A Phase IIb four-arm open-label randomised study to assess the safety and efficacy of h-R3 monoclonal antibody against EGFR in combination with chemoradiation therapy or radiation therapy in patients with advanced (stage III or IVA), inoperable head and neck cancer. J Clin Oncol 7:15s 2009 (suppl: abstr 6041).

potentially all tumours with their own vasculature. In contrast to other VDAs in development, CYT997 has been shown to be administrable orally as well as intravenously (iv)[2]. Oral dosing could differentiate CYT997 from other VDAs (see Exhibit 6) in terms of patient and hospital convenience. The concept of a low metronomic (ie, continuous) dose to follow an initial iv bolus could be used to reduce spikes in circulating epithelial precursor cells and potentially confer an efficacy advantage.

The potential first-in-class VDA, Antisoma's vadimezan (ASA404), failed Phase III interim analyses in first- and second-line non-small cell lung cancer in November 2010, and its commercial development has effectively ended. ASA404 remains in an investigator-sponsored 57-patient Phase II study in small-cell lung cancer.

Exhibit 6: Vascular disrupting agents in clinical studies

Product	Company	Notes
Ombrabulin (AVE8062)	Sanofi-Aventis	300-pt Phase II/III in advanced-stage soft tissue sarcoma after failure of anthracycline and ifosfamide (results: Oct 2011). 85-pt Phase I in combination with platinum-taxane doublet in advanced solid tumours is complete (no data announced).
Zybrestat (fosbretabulin)	OXiGENE	Enrolment complete in 180-pt Phase II/III (FACT) study with carboplatin/paclitaxel in anaplastic thyroid cancer, Phase II advanced platinum-resistant ovarian cancer, and 60-pt Phase II (FALCON) study with carboplatin, paclitaxel and bevacizumab in NSCLC (data at 22nd EORTC-NCI-AACR symposium). In combination with bevacizumab in Phase II 105-pt relapsed ovarian cancer study (results: early 2013).
BNC105	Bionomics	60-pt Phase II in mesothelioma pts unresponsive to pemetrexed + cisplatin (results due 2012). 152-pt Phase II of BNC105 + everolimus in second-line mRCC and BNC105 alone in pts progressing on everolimus (final results due 2012).
Plinabulin (NPI-2358)	Nereus Pharma	180-pt Phase I/II (ADVANCE) in combination with docetaxel in advanced NSCLC (completion due June 2011).
Verubulin (Azixa)	EpiCept/ Myrexis	128-pt Phase II study in glioblastoma multiforme (completion due Oct 2013). 68-pt Phase I/II open-label GBM trial completed. 30-pt Phase I/II in combination with carboplatin in recurrent/relapsed GBM ongoing, and 22-pt Phase I/II study with temozolomide in metastatic melanoma complete.
ABT-751/ E-7010	Abbott/ Eisai	Oral agent. 88-pt Phase II study in refractory neuroblastoma (results: January 2012). 165-pt Phase II study in combination with pemetrexed in advanced NSCLC did not show efficacy. Phase I/II in relapsed/paediatric ALL and Phase II studies in NSCLC with taxotere, lung cancer with carboplatin, and refractory haematological malignancies terminated.
OXi4503	OXiGENE	63-pt Phase I/II in relapsed/refractory carcinoma with hepatic tumours (results: July 2011). 40-pt Phase I dose-escalation study ongoing in patients with advanced solid tumours.
CYT997	YM Biosciences	Oral agent. 35-pt Phase Ib/II study in glioblastoma multiforme due to report data in H211. Two Phase I trials completed.
MN-029	Medicinova	Two Phase I trials in solid tumours completed. Non-core project.
Crolibulin (EPC-2407)	EpiCept	33-pt Phase I in advanced cancer completed. Phase Ib combination trial with other chemotherapies planned.

Source: Edison Investment Research

CYT997 has completed two Phase I studies: iv formulation data were presented at ASCO 2008, and results from the oral study were presented at ASCO 2009. Both studies and formulations showed good tolerability and preliminary signs of efficacy, as determined by tumour vasculature disruption measures. In the 31-patient iv study, 17 of 22 evaluable end-stage patients achieved stable disease through four cycles of therapy; in the oral capsule study, CYT997 demonstrated good absorption and linear dosing, with 12 of 21 patients showing stable disease in six weeks.

A 35-patient Phase Ib/II study in relapsed glioblastoma multiforme (a highly vascular tumour indication) is ongoing in Australia, using CYT997 iv in combination with carboplatin every three weeks. Patient recruitment was completed in early 2011, and the study is due to yield preliminary results in H211. A single-arm, open-label, Phase II study in relapsed and refractory multiple myeloma (NCT00664378) was terminated owing to the difficulty of patient enrolment.

[2] Francesconi A et al. Phase I evaluation of orally administered CYT997, a novel cytotoxic vascular-disrupting agent, in patients with advanced cancer. J Clin Oncol 27:15s, 2009 (suppl; abstr 3568).

Sensitivities

The potential market size for myelofibrosis and other myeloproliferative neoplasms will depend on YM BioSciences' and other companies' ability to charge premium prices, and the share of that market that CYT387 can seize is a key variable in our valuation methodology for YM (see below).

Additionally, YM is subject to sensitivities common to other biotech companies. There is risk associated with all clinical studies in that they might fail to demonstrate efficacy or might yield ambiguous/contradictory results; regulatory reviews are delayed or do not result in approval; and launched products fail to compete commercially. As no related up-front or milestone payments under potential future deals on either nimotuzumab CYT387 or CYT997 are factored into our model, these represent potential upside to our assumptions.

With respect to nimotuzumab, the US economic embargo on trade with Cuba is the most important sensitivity, despite YM's economic interests in nimotuzumab including substantial non-US territories. A clear path to US launch would require an exemption to this embargo.

It is also possible that the perceived complexity of the nimotuzumab development consortium might deter licensees/acquirers (other than Daiichi Sankyo). Improvement and scale-up to the licensor's manufacturing processes to support larger trials or commercial supply are an additional risk for nimotuzumab. However, as it is already marketed in 24 countries including India, China, Argentina, Brazil and Mexico, this suggests that YM's development risk is reduced.

Valuation

We continue to value YM on a risk-adjusted NPV basis, taking the three key pipeline projects in selected indications, assuming a base cost of running the business and applying a 12.5% cost of capital. For nimotuzumab, we assume a 20% gross pay-away to CIMAB and to Therapure BioPharma for manufacturing, and we assume that CYT387 and CYT997 are licensed out after Phase II studies on terms that include 19-20% royalties on sales. Following YM's discontinuation of the nimotuzumab study in NSCLC brain metastases we have removed this indication from the valuation matrix. Given the undisclosed nature and complexity of the various licensing deals YM has signed with members of the nimotuzumab consortium, in addition to the lack of visibility on much of the development and path to approval, we have attempted to value nimotuzumab only in those indications with most visibility.

CYT387 is now the major input in the valuation model for YM, and the potential market size (dependent on pricing) is a key sensitivity. We assume a current potential market worth $500m to $750m for the first indication, myelofibrosis. Other myeloproliferative neoplasms, such as polycythemia vera and essential thrombocythemia, represent bigger indications that could take the potential market to $2bn and beyond.

The possible share that CYT387 could seize is an important valuation input, and the drug will rely on projects ahead of it in development to establish the market. While 25% market share could be realistic initially, a key benefit will be the anaemia effect demonstrated by CYT387, and this might take the share up to 50% in a bullish scenario. Taking a mid-case view (37.5% share) and applying standard risk adjustments appears to support YM's current market cap (Exhibit 7).

Exhibit 7: YM BioSciences base-case valuation inputs

Product(s)	Status	Probability of success	Est launch year	Est peak market share	Current market value	Est maximum royalty	Est peak sales
CYT387 - JAK-1/JAK-2 inhibitor	Phase I/II	30%	2016	38%	$2,000m	19%	$2,089m
Nimotuzumab (EU - adult glioma)	Phase III	65%	2014	30%	$1,000m	15%	$481m
Nimotuzumab (EU - DIPG)	Phase II	30%	2015	30%	$500m	15%	$241m
Nimotuzumab (Asia - head & neck cancer)	Phase II	30%	2015	30%	$500m	15%	$234m
Nimotuzumab (Japan - gastric and NSCLC)	Phase II	30%	2015	30%	$500m	15%	$234m
CYT997 - tumour VDA	Phase Ib/II	30%	2016	5%	$5,000m	20%	$413m

Total rNPV	C$332m
Mar 2011 net cash	C$74m
Total valuation	C$405m

Source: Edison Investment Research

However, applying the same 30% risk adjustment and assuming a 50% market share yields a valuation of C$474m. As CYT387 advances through development, higher probabilities of success will be assigned to it, crystallising further value for YM and backing the investment case. The value of recent JAK inhibitor licensing deals could justify a further premium to our base-case scenario.

Financials

YM reported a balance of cash and equivalents of C$73.5m at its fiscal third-quarter end (31 March 2011), largely thanks to a fund-raising in December 2010 that brought in net proceeds of C$43.3m, including the exercise of an over-allotment option. The exercise of certain options and warrants raised a further C$1.8m in the nine-month period.

The company reported nine-month revenues of C$811,000, mainly from the deferred recognition of an upfront payment received in 2006 from Daiichi under a licensing deal for nimotuzumab, and the remainder in royalty income from limited sales of nimotuzumab in Europe. Because of a change in the estimated duration of the Daiichi collaboration, the revenue recognition period has been extended by three years to July 2015, and this has been built into our financial model.

Following the takeover of Cytopia in February 2010, YM reported a sharp increase in nine-month R&D spending and administrative costs, at C$15.7m (68%) and C$7.4m (45%) respectively. This was also due to restructuring and the addition of an Australian office. We have accordingly raised our forecasts for FY11 and FY12 operating costs.

As of 30 April 2011, YM had 116.5m common shares outstanding, together with 7.4m warrants priced at C$1.60 each and exercisable at any time until 10 March 2015. Given YM's current share price these warrants are well in the money, and we accordingly expect all of them to be exercised. For convenience, our financial model (Exhibit 8, below) shows the effect of this warrant exercise in FY12, giving rise to an extra C$11.9m in financing and taking the total number of YM common shares outstanding up to 123.9m.

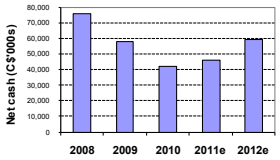
In April 2010, YM signed a controlled equity offering with Cantor Fitzgerald under which it can, at its discretion, sell up to 7.75m shares at prevailing market price. During the third quarter, YM sold 500,000 shares through this programme, resulting in net cash proceeds of $1.2m. So far in Q411 it has sold another 5.2m shares, bringing in $12.1m net.

We expect YM to finish the current fiscal year with cash of C$74m, and our model shows the company to be financed well beyond FY12.

Exhibit 8: YM BioSciences' financial model

C$'000 Year end 30 June	2008 Cdn GAAP	2009 Cdn GAAP	2010 Cdn GAAP	2011e Cdn GAAP	2012e Cdn GAAP
PROFIT & LOSS					
Revenue	**4,859**	**4,543**	**2,611**	**1,188**	**880**
Cost of sales	0	0	0	0	0
Gross profit	4,859	4,543	2,611	1,188	880
EBITDA	**(14,355)**	**(12,556)**	**(17,276)**	**(23,216)**	**(22,178)**
Operating profit (before GW and except.)	**(14,480)**	**(12,648)**	**(17,340)**	**(23,295)**	**(22,258)**
Intangible amortisation	(1,061)	(1,061)	(2,939)	(4,508)	(4,000)
Exceptionals	0	0	0	0	0
Stock option charges	(1,929)	(427)	(799)	(2,502)	(1,500)
Operating profit	**(17,470)**	**(14,135)**	**(21,078)**	**(30,306)**	**(27,758)**
Net Interest	2,584	1,070	84	412	250
Profit before tax (norm)	**(11,896)**	**(11,578)**	**(17,256)**	**(22,883)**	**(22,008)**
Profit before tax (Cdn GAAP)	**(14,886)**	**(13,065)**	**(20,993)**	**(29,894)**	**(27,508)**
Tax	0	(4)	0	0	0
Profit after tax (norm)	**(11,761)**	**(11,248)**	**(17,071)**	**(23,601)**	**(22,008)**
Profit after tax (Cdn GAAP)	**(14,886)**	**(13,069)**	**(20,993)**	**(29,894)**	**(27,508)**
Average number of shares outstanding (m)	55.8	55.8	63.6	98.4	120.2
EPS - normalised (C¢)	(21.1)	(20.1)	(26.8)	(24.0)	(18.3)
EPS - Cdn GAAP (C¢)	(26.7)	(23.4)	(33.0)	(30.4)	(22.9)
Dividend per share (C¢)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed assets	**4,194**	**3,102**	**11,730**	**9,501**	**9,521**
Intangible assets	4,065	3,005	11,646	9,392	9,392
Tangible assets	128	97	85	109	129
Investments	0	0	0	0	0
Current assets	**58,879**	**42,968**	**46,044**	**74,788**	**59,147**
Debtors	403	565	161	295	295
Cash	58,101	42,051	45,645	74,102	58,461
Other	375	353	238	391	391
Current liabilities	**(6,646)**	**(3,191)**	**(4,309)**	**(4,276)**	**(4,276)**
Creditors	(308)	(431)	(699)	(974)	(974)
Accrued liabilities	(1,715)	(487)	(2,086)	(2,734)	(2,734)
Deferred revenue	(4,623)	(2,273)	(1,524)	(568)	(568)
Tax and social security	0	0	0	0	0
Short-term borrowings	0	0	0	0	0
Long-term liabilities	**(4,414)**	**(2,039)**	**(1,651)**	**(1,703)**	**(1,135)**
Long-term borrowings	0	0	0	0	0
Other long-term liabilities	(4,414)	(2,039)	(1,651)	(1,703)	(1,135)
Net assets	**52,013**	**40,840**	**51,815**	**78,309**	**63,256**
CASH FLOW					
Operating cash flow	**(20,056)**	**(17,018)**	**(16,828)**	**(30,271)**	**(27,678)**
Net interest	2,584	1,070	84	412	250
Tax	0	0	0	0	0
Capex	1	(60)	(41)	(92)	(100)
Expenditure on intangibles	0	0	0	0	0
Acquisitions/disposals	0	0	0	0	0
Financing	0	(42)	19,469	58,408	11,887
Dividends	0	0	0	0	0
Net cash flow	(17,471)	(16,050)	2,685	28,457	(15,641)
Opening net debt/(cash)	**(75,572)**	**(58,101)**	**(42,051)**	**(45,645)**	**(74,102)**
HP finance leases initiated	0	0	0	0	0
Other	0	0	910	0	0
Closing net debt/(cash)	**(58,101)**	**(42,051)**	**(45,645)**	**(74,102)**	**(58,461)**

Source: Edison Investment Research

Growth	Profitability	Balance sheet strength	Sensitivities evaluation	
N/A	N/A		Litigation/regulatory	●
			Pensions	○
			Currency	◖
			Stock overhang	○
			Interest rates	○
			Oil/commodity prices	○

Growth metrics	%	Profitability metrics	%	Balance sheet metrics		Company details	
EPS CAGR 07-11	N/A	ROCE 10e	N/A	Gearing 11e	N/A	Address:	
EPS CAGR 09-11	N/A	Avg ROCE 07-11	N/A	Interest cover 11e	N/A	5045 Orbitor Drive, Bld 11, Suite 400, Mississauga, Ontario L4W 4Y4, Canada	
EBITDA CAGR 07-11	N/A	ROE 2011e	N/A	CA/CL 11e	N/A		
EBITDA CAGR 09-11	N/A	Gross margin 11e	100	Stock turn 10e	N/A	Phone	+1 905 629 9761
Sales CAGR 07-11	N/A	Operating margin 11e	N/A	Debtor days 11e	N/A	Fax	+1 905 629 4959
Sales CAGR 09-11	N/A	Gross mgn/Op mgn	N/A	Creditor days 11e	N/A	www.ymbiosciences.com	

Principal shareholders	%
Baker Bros Advisors	8.2
Balyasny Asset Management	5.1
Pyramis Global Advisors Trust	4.0
Federated Investors	2.7
Healthcor Management	2.7
Deerfield Management	2.2
Ridgeback Capital Investment	1.7

Forthcoming announcements/catalysts	Date
Fiscal 2011 results	September 2011
Full data from CYT387 Phase I/II study	By end-2011*
Estimated	

Management team

President and CEO: Dr Nick Glover (British)

Joined YM as president and CEO in 2010. Before that he was president and CEO of Viventia Biotech, a company that he joined in 2000 as Director of Corporate Development. Previously he was an investment manager at a VC firm. He has authored or co-authored more than 50 scientific papers.

Chairman: David Allan (Canadian)

Has been Chairman since 1994, and was CEO from 1998 to 2010. Earlier, he founded the knowledge-based industries group of a Canadian investment bank, and was a governor of the Toronto Stock Exchange and a member and working group Chair of the Ontario Biotechnology Advisory Board.

Chief scientific advisor: Dr Christopher Burns (Australian)

Joined YM through the takeover of Cytopia, where he had worked since 2001. Previously worked at Pfizer Central Research in the UK and in academia. Currently serves as a faculty member at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia.