24 October 2011

Aastrom Biosciences

Year End	Revenue ($m)	PBT* ($m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/10	0.89	(17.7)	(71.7)	0.0	N/A	N/A
12/10 +	0.25	(11.6)	(39.7)	0.0	N/A	N/A
12/11e	0.00	(27.4)	(71.1)	0.0	N/A	N/A
12/12e	0.00	(33.6)	(86.9)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation and exceptional items.
+ Aastrom changed its financial year giving a six month July-Dec 2010 reporting period.

Investment summary: Leg-saving cell therapy

Aastrom has developed a patient-specific cell therapy using a proprietary cell culture process. Its lead project in Critical Limb Ischaemia (CLI) aims to increase amputation-free survival in patients with blocked leg arteries. Strong Phase II data, to be fully reported 12-16 November, has led to a pivotal 594 patient Phase III starting Q411. A dilated heart indication has Phase II data with Phase IIb starting H112.

Technology: Patient-specific (autologous) cell therapies

Aastrom's autologous cell therapy, ixmyelocel-T, takes a bone marrow aspirate from a patient and cultures it using a proprietary process. This boosts the numbers of healing stem cells and macrophages. Cells are returned to the patient and injected near the disease site. This process minimises safety issues and only takes 12 days.

Critical data on CLI

The initial report from the 86 patient RESTORE-CLI Phase IIb trial in June showed a statistically significant reduction in amputations and amputation-related risk factors. Full data will be published 12-16 November. The pivotal Phase III in 594 patients has been FDA agreed under an SPA. If ixmyelocel-T meets the 12 month, amputation-free survival endpoint, it should be the first marketed cell therapy for CLI and the only treatment option for 100,000-150,000 potential amputees per year in the US.

Dilated hearts; new hope for an intractable problem

Aastrom's next ixmyelocel-T project is in dilated cardiomyopathy (the heart muscle is weakened and distends giving poor circulation). Phase IIa 12 month clinical data indicated good safety and responses in the ischaemic form of the disease. Further trials using catheter delivery should start in 2012. This could be a large market.

Valuation: Standalone US strategy with EU partner?

Aastrom plans to market directly to c 3,000 US vascular surgeons to maximise returns. We assume an EU partnering deal. This strategy at a $25,000 price gives an indicative value of $8.90 a share. However, further funding will be needed to fund Phase III trials indicating a realistic $6 a share depending on the funding mix.

Price	$2.38
Market Cap	$92m

Share price graph

Share details

Code	ASTM
Listing	NASDAQ
Sector	Biotech
Shares in issue	38.6m

Price

52 week	High	Low
	$4.45	$1.39

Balance Sheet as at 30 June 2011

Debt/Equity (%)	N/A
NAV per share (c)	(26)
Net borrowings ($m)	0.04

Business

Aastrom Biosciences uses autologous cell therapy to process and inject the patient's own cells. The lead Phase III product aims to reduce the amputation rate in patients with blocked leg arteries: this has $1.25bn sales potential. A dilated cardiomyopathy indication has completed a Phase II trial and will start Phase IIb in ischaemic disease in H112.

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
N/A	N/A	N/A	N/A

Analysts

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Investment summary: Leg-saving cell therapy

Company description: Leading cell therapy

Aastrom was founded in 1989 and listed on NASDAQ on 4 February 1997 at $7/share. It is based in Ann Arbor, Michigan. The current lead therapy, ixmyelocel-T, decreases the risk of amputation due to critical limb ischaemia (CLI); a second, earlier-stage project is for ischaemic dilated cardiomyopathy (ICM), a condition in which the heart is distended and weakened. Aastrom uses a proprietary system to boost the numbers of stem cells and macrophages obtained from the patient's bone marrow. The cells are grown in a centralised production facility capable of producing 3,000 treatments per year, enough for the projected clinical programme. Regulatory aspects are key as precedents are few and clinical data generally limited. Gaining an FDA SPA on the design of the CLI Phase III was a crucial milestone for Aastrom that gives a faster route to product registration. Aastrom had invested $237m to 30 June 2011; $22.5m was raised in H210.

Valuation: Direct US sales yield high returns; EU might be partnered

Currently, Aastrom plans to market directly to approximately 3,000 US vascular surgeons to maximise returns. A US partner would bring cash but Aastrom will have more expertise and the market is very focused. We assume an EU partnering deal as national European pricing negotiations will be tedious. This strategy at a $25,000 price gives an indicative value of $8.90 a share with a 50% CLI Phase III risk adjustment. However, further funding of $30m per year from 2012 will be needed to fund Phase III, indicating a realistic $6 per share value, depending on the funding mix.

Sensitivities: Cutting the market to size

Aastrom offers high upside given the growing CLI market and solid Phase IIb data released so far. The clinical risk lies in the use of the harder amputation-free survival endpoint in Phase III, which was only indirectly tested in Phase IIb. The use of a more ill patient group makes events more likely, but raises the therapeutic hurdle that ixmyelocel-T has to achieve. To achieve $1bn+ revenue, ixmyelocel-T needs to show enough amputation-free survival improvement to establish a $25,000 price point with at least 33% of eligible patients treated. The Terumo (Harvest) device could enter the market, which could disrupt the market for cultured cells and might limit it to severe cases. The ICM indication has good exploratory data but needs confirmation is statistically powered studies.

Financials: Cash needed to run the pivotal trial

Aastrom's Q2 SEC filing shows an annualised burn rate of $25m (based on $12.6m in H1); this has risen from $17m in calendar 2010, possibly due to costs attached to the impending CLI Phase III study. Cash on 30 June was $18.5m after the $20.6m net equity funding in December 2010. A new funding round will be needed, possibly after starting the CLI Phase III and ideally after publishing RESTORE final data to enable a full evaluation of Phase III prospects.

Company description: Leading cell therapy

Aastrom is based around a cell culture process using disposable cassettes (Exhibit 1).[1] To produce ixmyelocel-T, harvested bone marrow cells, taken as an aspirate from individual patients, are cultured for 12 days at a central facility in Michigan. These are then shipped back to the patient for injection near the disease site as an autologous, (patient specific) therapy. The initial indication was regeneration of bone marrow after cancer chemotherapy. Aastrom then evaluated bone regeneration but this was deprioritised in 2008. The lead ixmyelocel-T, project is now to reduce the risk of leg amputation due to severe Critical Limb Ischaemia (CLI). This is about to enter a Phase III that the FDA has agreed under a Special Protocol Assessment (SPA). This could allow approval based on only this study. A further project, in Phase II, is in dilated cardiomyopathy. Competition is from other start-ups. Major pharma has academic collaborations and is watching biotech developments in the cell area. We expect big Pharma deals on viable indications like CLI.

Cell therapy: Background and status

Cell therapies, an attractive therapeutic concept, have been feasible in theory for some decades and many, usually small, companies are trying to develop them. In addition, there are a lot of academic trials, often in collaboration with major Pharma companies. Deals in the area have been sparse, the major one being the December 2010 Cephalon-Mesoblast tie-up with a headline $2bn value; this might unravel with the Teva bid for Cephalon. However, the area has yet to break into mainstream therapy despite its huge potential. In the US, three cell therapies have been approved by the FDA:

- Carticel (autologous cultured chondrocytes) for cartilage repair (Genzyme, 1997);
- a cell-based melanoma vaccine, Provenge (sipuleucel-T) from Dendreon in 2010; and
- a cosmetic therapy laViv (azficel-T) from Fibrocell Science to treat nasolabial folds approved June 2011.

All these are autologous, that is they use a cultured version of the patient's own cells. Doses are individually prepared, which can take two to 22 weeks depending on the product. This makes the therapy expensive. The alternative is therapy based on cell lines produced in culture (allogenic).[2] In theory, these standardised products could be cheaper. As none has reached the market, this is hard to confirm.

Product: Tissue repair cells

Aastrom's ixmyelocel-T uses the patient's own cells. To start, a needle is inserted into the patient's hip bone to extract a 50ml sample of bone marrow. This is an outpatient procedure. The bone marrow aspirate is then sent to a central processing facility in Ann Arbor, Michigan. Since the therapy is derived from the patient, the source material will obviously vary in quality. At the facility, the cells are grown in a special incubator using disposable cartridges and standard conditions (Exhibit 1, A-C). Cell expansion changes the composition of the cell populations (Exhibit 1D). The

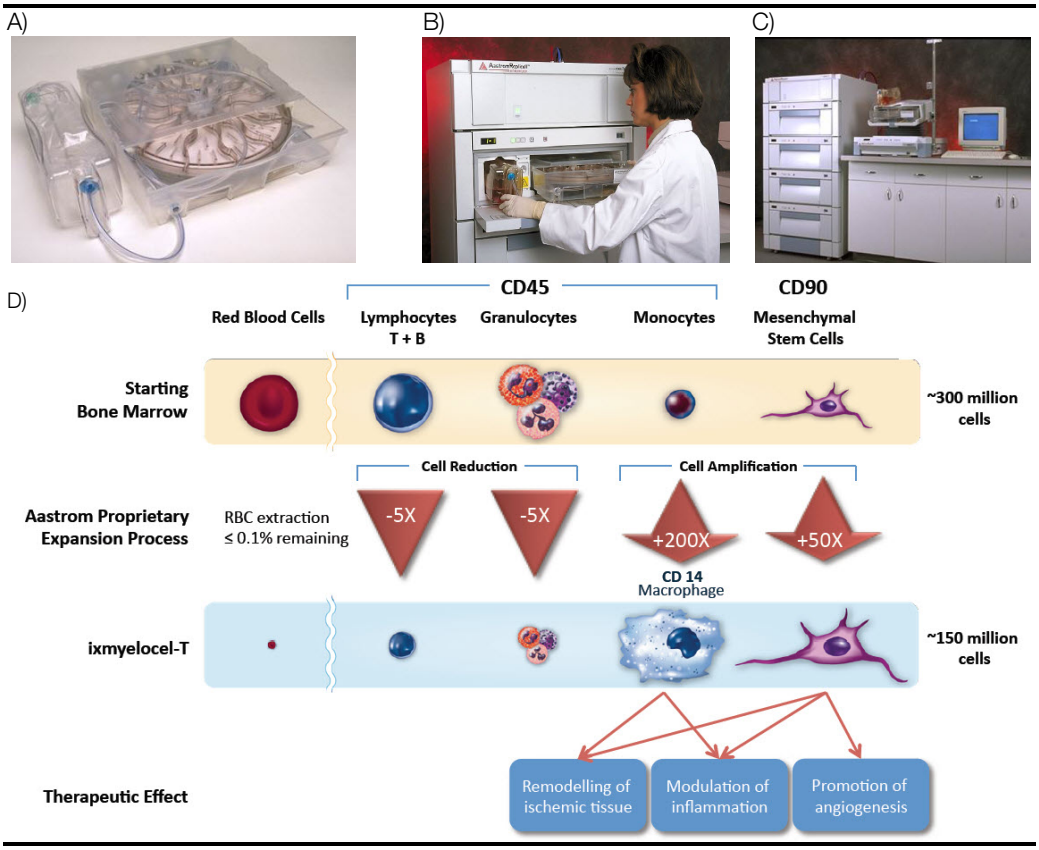
[1] Direct sales of the cassettes as a research product ended in 2004. Plans to develop this process as a clinical a point-of-care system were not viable.

[2] These are typically derived from pluripotent foetal cells and so more controversial. Allogenic products are, in theory, commercially more attractive with a standardised product (the same number of the same cell type each time) , broader market and the potential for product to be kept at the hospital offering immediate treatment. However, allogenic product development faces additional and tougher safety hurdles, like immunogenicity, and the need to produce a consistent cell product over many years.

number of cells resulting will vary with the patient sample[3] as the processing conditions are standardised and not optimised per individual. Ann Arbor can currently process up to 3,000 patient samples per year.

Exhibit 1: Aastrom Replicell culture system

A) Bone marrow from individual patients is cultured in the sealed, aseptic culture cassette. This is not a telephone but a bag of culture medium. B) Individual cassettes are loaded into the incubator unit where they are incubated for 12 days. C) Scale up requires adding more incubation units. D) Changing cell composition.



Source: Aastrom

To administer the product, it is shipped overnight to the hospital. The cells are injected in small equal aliquots around the lower leg and foot.[4]

Critical limb ischaemia: Lead Phase III indication

The initial manifestation of peripheral artery disease is usually intermittent pain due to arterial blockage, known as intermittent claudication (IC). The condition is usually part of a general atherosclerotic condition. In severe cases, a major artery is mostly or totally blocked leading to critical limb ischaemia (CLI). The 15-year mortality for patients with IC is 70%, mostly from coronary artery disease. CLI restricts walking and any cuts or bruising on the foot or lower leg can give rise to ulcers that fail to heal due to poor blood supply. This is a problem in advanced-stage diabetes; diabetic ulcers are very demanding to nurse. If gangrene infects the wound, amputation follows.

[3] This variability may affect clinical outcomes in individual patients. In regulatory terms, the key factors are the system reliability; ensuring that patients get their own cells back; and there is no contamination at any stage.
[4] A typical pattern is five equidistant equal injections in bands around the lower thigh, upper calf, mid calf, just above the ankle and if appropriate also between the bones of the foot. This is 20 small injections. There is no repeat dosing. We are not aware of any optimisation of this. Aastrom has some internal data to suggest that cells migrate from the injection sites.

Conventional treatments

Most claudication patients are treated with exercise and drugs. Cilostazol (branded Pletal) and Pentoxifylline (branded Trental by Aventis) improve lower leg blood supply in c 25% of patients. Atherosclerosis and thrombosis risk is managed with lipid lowering and antiplatelet drugs like Lipitor (atorvastatin) and Plavix (clopidogrel). Risk factors like smoking and obesity need management.

The major objective of surgical revascularisation is limb preservation. Historically, this involved major surgery to remove diseased arteries and replace them with harvested veins, usually a greater saphenous vein bypass. Over 100,000 vascular reconstructive procedures are performed each year in the United States alone.[5] This is a major, but generally effective, operation that cannot be tolerated by every patient and will only be used if a major leg artery is totally or heavily occluded.

Increasingly, peripheral angioplasty is used both instead of a bypass and in many patients who otherwise would not be treated.[6] The patency rate, the time the artery stays open, is around 80% for a year after angioplasty but the procedure can be repeated as required; patency does not necessarily translate into a successful clinical outcome however (eg Taylor *et al* 2007).

RESTORE-CLI: A successful Phase IIb

Aastrom has run the biggest cell therapy trial in CLI to date.[7] This was a double-blind, placebo-controlled Phase IIb study with 72 treated patients recruited across 18 US medical centres.[8] These patients had no further treatment options. The primary endpoint at Phase IIb was a composite based on the absence of any of the following four events (only the first event counts): a doubling of the wound area; new gangrene; amputation; or death.

Aastrom convincingly argues that a doubling of wound (ulcer) size or new gangrene is a good leading indicator of treatment failure that will lead at some point to amputation. Use of the composite endpoint led to enough events for the Phase II readout but may not be fully reflective of eventual Phase III outcomes. The trial was not statistically powered to be significant on the amputation-free survival endpoint usually required for registration, here treated as secondary; this hard endpoint will be used for the Phase III. There have been three analyses done, Exhibit 2. The first analysis was in February 2010 and is published. A further analysis was done in November 2010, and has been presented but not published. The top line 12 month data on all patients was reported in June 2011. Full data will be presented at the American Heart Association meeting 12-16 November 2011 and published in a peer reviewed journal.

By the second interim analysis 72 patients had completed over six months follow up: 48 active, 24 placebo. There was a clear separation in the primary endpoint of time to first event, Exhibit 3A, with 20 events in the treated group (42%) compared to 15 events in the control group (63%).

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[5] Stillman, RM. Infrainguinal Occlusive Disease: Treatment. Medscape Article 460965.
[6] Cordis has refocused its business with greater focus on peripheral artery products. Bard acquired ClearStream to build a position in this area. Abbott is developing a new dissolvable lower-leg stent for CLI. It is likely that the increasing use of lower limb angioplasty in the US will change the number of amputations, but there will always be patients who are untreatable by this route.
[7] Powell, RJ, *et al.* Interim analysis results from the RESTORE-CLI, a randomized, double-blind multicenter phase II trial comparing expanded autologous bone marrow-derived tissue repair cells and placebo in patients with critical limb ischemia. J Vasc Surg.2011 Jun 18.
[8] The recruitment target was 150; this was reduced after the first interim analysis as the efficacy appeared higher than expected

Exhibit 2: RESTORE patient numbers and outcomes as disclosed to date

Note: Interim analyses used patients surviving over six months since treatment or with endpoints and at one year for the final data set.

Date	Treated patients			Time to failure (any cause)	Amputation-free survival
	1 year	1 year to 6 mths	6 mths> or withdrew		
February 2010	33	13	40	0.0053	0.038
November 2010	62	10	14	0.0132	0.5541
June 2011 (Final)	72	0	14	<0.13	Not significant

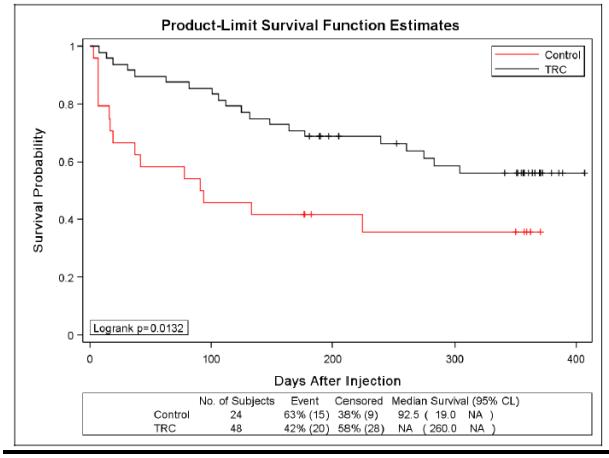
Source: Aastrom press releases, Powell, RJ *et al.* J. Vasc. Surg. 2011, November 2010 VEITH symposium and Edison estimates

However, in terms of the secondary endpoint of amputation free survival, Exhibit 3B, although the control patients had a high event rate at the first analysis there was then a zero event rate between the first and second analyses (in total seven events, 29%). In contrast, the treated group had a constant event rate (totalling 12 amputations or deaths, 25%). This gave a non statistically significant difference, p=0.55. This is typical statistical noise in a small trial with multiple analyses. The hazard ratio (a measure of the change is risk) showed that amputation or death was 24% less likely if treated - although the error range is extremely wide on these small numbers.

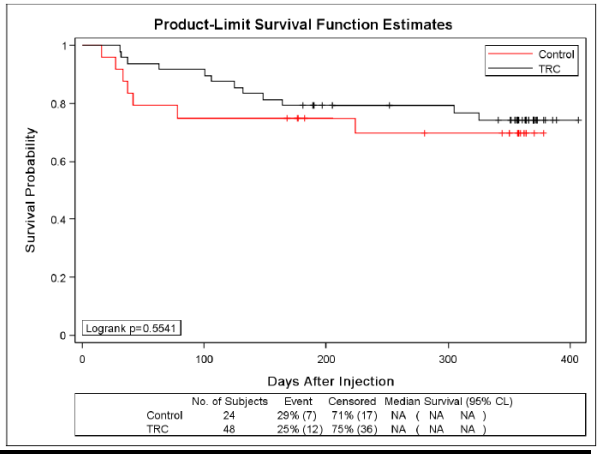
Exhibit 3: Second interim analysis data from RESTORE-CLI

These charts show the probability of an event occurring at a particular time point. As this is interim data, it is censored to reflect the different times that patients have been in the study without experiencing an event (times shown by a vertical bar). Each event is marked by a drop in the probability line, for example, the red, control, line in 3B shows seven steps each marking the time of an amputation or death. There were a large number of events on the control groups early in the study (3A).

A) Progression from any cause or death



B) Amputation-free survival



Source: Powell RJ *et al.* *Presentation of Second interim Analysis*

In the limited full 12-month data set, the primary outcome was strongly positive and statistically significant. The value was better than in the second interim analyses (p=0.0132). The control amputation rate rose, but this secondary measure will not be statistically significant. The Phase IIb data appears strong and convincing but Phase III cannot be taken for granted.[9]

CLI Phase III design and outlook

Although the FDA has accepted the Phase II as robust, Aastrom's hypothesis that the Phase IIb composite primary endpoint reflects eventual amputation risk has not been confirmed statistically. The Phase III design is randomised, double-blinded, and placebo-controlled. It aims to recruit up to 594 patients at approximately 80 US clinical sites. The enrolled patients will have no treatment options apart from amputation and all will have tissue loss on enrolment (due to wounds and /or

[9] A Phase II gene therapy study in CLI (NV1FGF, Vical/Sanofi designed to promote angiogenesis) cut the amputation rate by half (a secondary endpoint) but the subsequent TAMARIS Phase III failed to show efficacy. Belch, J. *et al.*. The Lancet, 2011:377; 1929 – 1937.

gangrene). This makes them high-risk cases as these patients are five times more likely to experience an amputation within 12 months of diagnosis.[10] Aastrom emphasises that tissue loss indicates a higher amputation risk.

On 26 July 2011, Aastrom announced that the FDA had accepted the Phase III design under a Special Protocol Assessment: if the endpoint is reached, this trial will be sufficient for approval. The trial is expected to start in Q411. Results could be announced in 2014 with marketing from 2015.

CLI competition

Aastrom is a leading player in a development area where clinical progress has been slow. The cell therapy area has many emerging companies, notably Pluristem (NASDAQ, Israeli) and Harvest Technologies. Exhibit 4 gives a brief overview of CLI cell therapy development projects.

Exhibit 4: CLI cell therapy development projects

Company	Stage	Comments	Data due
Aastrom Biosciences	Phase III in 594 patients	The RESTORE 86 patient Phase II showed statistical significance on a composite endpoint. Autologous cells are bone marrow derived and are cultured in a central facility. Endpoint of amputation-free survival	Phase III starting Q411, data 2014?
Harvest Technologies (Terumo)	Phase III at 23 US centres in 210 patients	Uses a bedside collector (SmartPReP 2 BMAC) to harvest stem cells from bone marrow aspirate within 15 minutes. Concentrated cells are immediately injected into the leg. Terumo acquired in 2011 for $70m.	Phase III started in May 2011 with data mid 2014.
Arteriocyte (US)	Phase I 10 patient safety	Uses Magellan cell processing system to harvest autologous cells. Endpoint is amputation or death within 12 months.	Started in April 2011. Data maybe H113.
Apceth (Germany)	Phase I/II in 30 patients	Uses human Bone Marrow Derived Autologous, CD34-Negative Mesenchymal Stem Cells. Cells are administered after angioplasty.	Started March 2011. Data 2013.
Stempeutics (India)	Phase I/II in 20 patients	*ex Vivo* Cultured Adult Allogenic Mesenchymal Stem Cells. Largely safety with secondary data on efficacy	Report H112.
Pluristem (Israeli, US Listed)	Phase I dose ranging 15 pts Phase I 12 pts	Uses PLX-PAD cell. These are placental cells cultured in a proprietary reactor system. They are supposed to be immune modulatory. Tested single and double treatment courses each with multiple injections.	End date Oct 2011.

Source: Edison based on Clinicaltrials.gov data

Harvest has FDA approval for a device to collect bone marrow cells. They are planning a trial of an autologous therapy derived from bone marrow in which the cells are harvested at the patient's bedside; a centralised processing facility is not needed. However, there is no cell expansion stage so relatively small cell numbers may be used. Harvest was acquired in May 2011 by the medical equipment giant Terumo for $70m. Hence, it has the cash and resources to commercialise its system, if successful. The time line appears similar to Aastrom. The listed company with a high profile in the area is Pluristem, which has reported a 75% reduction in amputation rates in its current trials. Data is due Q411 and may enable a Phase III, although the trials seem small for this and a phase II may be needed. The most interesting might be Apceth, a German company. It uses a similar procedure to Aastrom with cultured bone marrow cells. These are being injected after angioplasty at the surgery site. The outcome ought to be applicable to Aastrom's product.

The costs of amputation are high surgically but especially in increased morbidly and long-term nursing and social costs. Hence, US insurers will be more willing to pay a high price if ixmyelocel-T prevents a significant number of amputations.

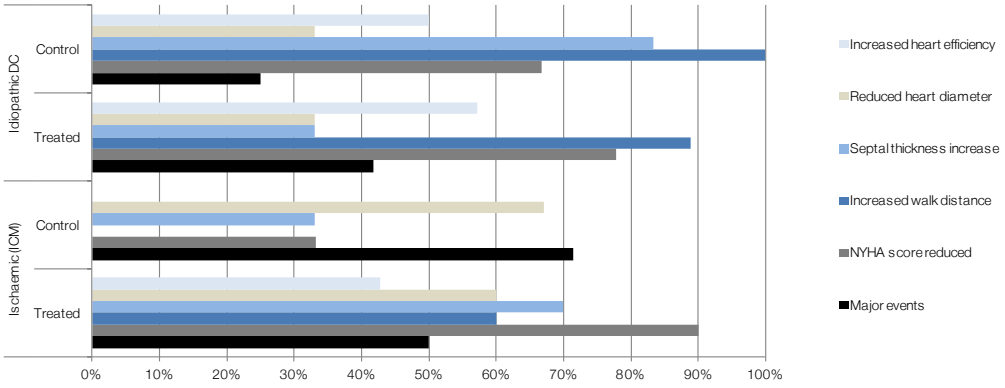
Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is a weakened and distended left ventricle of the heart. [11] Less blood is pumped per heartbeat and this leaves patients out of breath and tired. This leads to fluid

[10] Patients with rest pain in the leg but no tissue loss have a c 3% risk of amputation with a year. With tissue loss, the amputation rate is 17%. Use of only tissue loss patients improves the chances of a statistical result.

retention. Major events (arrhythmias, thromboembolism and sudden death) are common and may occur at any stage. DCM mostly manifests itself as heart failure in middle-aged men. There are two types of DCM: ischaemic (IDC) and idiopathic (ICM). IDC is only treatable by revascularisation and surgical removal of part of the heart to reduce left ventricle volume (the Batista procedure). In ICM, there may also be coronary disease but the heart is enlarged more than would be expected.[12] Full data has been reported from the exploratory IMPACT trial study in IDC and ICM (Exhibit 5).[13]

Exhibit 5: 12 month outcomes in ixmyelocel-T treated vs control patients in ischaemic (ICM) and idiopathic (IDC)



Source: Edison graph based on data presented at the 15th Annual Heart Failure Society of America Scientific Meeting 19 Sept. 2011

IMPACT enrolled 12 ICM and 12 IDC treated patients with seven and eight respectively in the control groups. The trial was not powered to be statistically significant. The ICM patients appeared to respond better than the IDC patients whereas the ICM control group fared worse with 71% of them (experiencing a major cardiac event. Hence, IDC seems a stronger indication than IDC for a Phase IIb although both may eventually be treated using ixmyelocel-T.

A further trial is testing catheter-based injection of cells. It has recruited 12 active and 12 placebo patients. Final data is due in H1 2012. Cather delivery is essential for commercial viability. Interim data suggests a functional improvement rate like that in IMPACT but with fewer adverse events.

A larger Phase IIb using catheter delivery will probably be run in ICM. It is possible that the FDA may review this trial under an SPA and agree that this study is adequate for approval. However, it is more likely that an extra Phase III study will be needed as neither study so far is statistically powered. We have no specific timeline on this. A market date of 2017-18 would seem realistic. Aastrom has orphan drug designation for this indication which can speed time to market.

Market size

The incidence of DCM may be seven in 100,000[14] with perhaps 9,000 US deaths per year.[15] This implies c 20,000 new cases per year in the US. However, the data is patchy and limited. Modern treatments mean that historic 50% mortality within two years of diagnosis is probably too high. Aastrom puts DCM US patient prevalence in the 150,000-400,000 range.

[11] Richardson P, et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the definition and classification of cardiomyopathies. Circulation 1996; 98: 841-2.
[12] ICM is separate to the common ischemic cadiomyopathy which is solely due to coronary artery disease and myocardial infarct; this can cause some ventricle dilation. It is treated by coronary angioplasty.
[13] Presented at the15th Annual Heart Failure Society of America Scientific Meeting September 19, 2011
[14] Rakar, S, *et al.* Epidemiology of dilated cardiomyopathy: A prospective post-mortem study of 5252 necropsies. European Heart J (1997) 18, 117-123.
[15] Gillum R F. Idiopathic cardiomyopathy in the United States, 1970-1982. Am Heart J 1986; 111: 752-5.

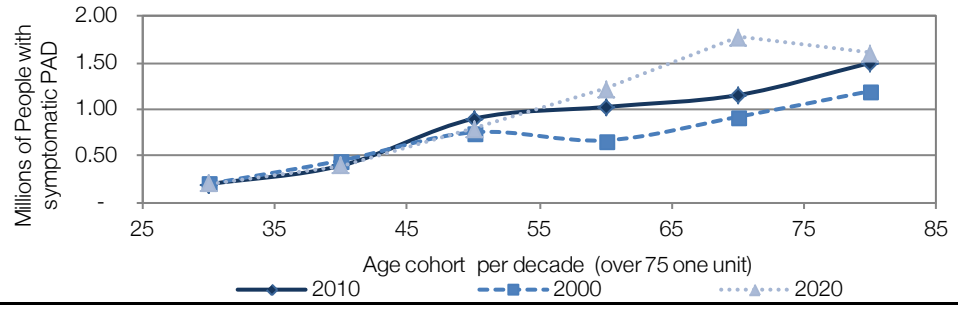
Valuation

The valuation is based on the single lead indication of CLI. We have not been able to value IDC at this stage of its development. The valuation model uses discounted cash flow analysis based on a sales and cost projection to 2025 assuming 2015 CLI approval and 2016 full launch. We have made a 50% risk adjustment to cover the Phase III CLI trial risk.

Nine million people in the US and about 18m in Europe may have artherosclerotic peripheral artery disease (PAD).[16] TASC-II[17] estimated that 25% of IC patients will progress to CLI within five years, 6-7% in the first year, and that 25% of CLI patients are eventually managed through amputation. Under 2% of total IC patients need amputation in any five-year period.

The rates of PAD are very age dependent. Treated PAD patients account for c 0.5% of the 30-39 age cohort rising to 3% of 60-64 year olds and 6% of the over 65-69 age group. Rates of PAD may reach 10-20% in those over 75. Many suffers from IC do not seek medical attention so the reported prevalence is much lower. We have plotted the probable age distribution in the US using 2000 census data for 2000, 2010 and 2020, Exhibit 6. The ageing baby boom generation should drive a rise in the diagnosed cases of IC from 4.2m in 2000 to c 5m now and around 6m in 2020.

Exhibit 6: Changing demographic profile of IC patients under medical care in the US



Source: US census data 2000, TASC prevalence rates by age and Edison modelling.

There are at least 97,000 lower leg amputations per year in the US due to vascular dysfunction.[18] We assume that many of these are due to diabetic conditions and leg ulceration. TASC claims that 1-3.3 % of IC patients need amputation within five years of diagnosis, but also notes that 25% of CLI patients have amputation as the primary treatment. Taking the IC figure of 5m patients, a 2% amputation rate equates to 100,000 patients per year. We have not assumed an expanded market at this stage but there are probably at least c 400.000 CLI patients who may be future targets for cell therapy. If 10% of these were treated each year, it would add an extra $1bn in sales. There are no specific health economic studies on ixmyelocel-T. Assuming a $25,000 price point, a probably low value[19], the potential high risk of amputation market by 2020 could be worth $2.5bn.

[16] Henry, T.D. *et al.* "POBA Pus" Will the balloon regain its lustre. Circulation 2008; 118: 1309-1311. Population estimates are 3% of 40+ year olds and 6% of 60+ year olds (TASC guidelines 2006).
[17] Trans-Atlantic Inter-Society Consensus for the Management of PAD (TASC-II).
[18] Amputee Coalition of America 2008 factsheet. The source for the data reported in this factsheet is a 2002 publication. It is often difficult to track specific procedure numbers across the whole US due to the fragmented state-level medical systems. The number might be over 150,000 in 2010.
[19] The two year costs of amputation were estimated in 2007 at $91,106 with a lifetime cost of $509,275; these costs may be higher for elderly diabetic patients. Hence, even small reductions in amputation rates could support higher prices and $30-50k might be feasible if the Phase III shows high efficacy in seriously at risk patient. Denderon is charging $93,000 per three treatment course of its ant-cancer cell therapy but this appears uncompetitive with J&J's oral Zytiga (Abiraterone) which has similar efficacy.

Currently, Aastrom plans to market directly to c 3,000 US vascular surgeons to maximise returns. We estimate that might need a 15-20 person sales and marketing team. This should cost $10m per year to run but our model assumes a cost equating to 15% of US sales: $30m in 2016. A US partner would bring cash and a sales force, but Aastrom will have more therapeutic expertise and the market is very focused. We assume an EU partnering deal as national European pricing negotiations will be long and tedious.

Our model assumes that by 2025, Aastrom is treating 41,000 patients per year in the US (c 34% share) with sales starting in the second half of 2015. This could generate $1.1bn per year plus 12.5% EU royalties (worth $70m due to lower EU pricing and market penetration).

Indicative value

On the above assumptions, the Edison model indicates an indicative value of $8.90 a share, including a nominal $10m IDC value. However, funding of $30-40m per year will be needed from 2012 until 2015 indicating a possible $6.1 a share after the extra funding requirement is deducted.

If the therapy price was $35k, the share value would rise to around $18 per share ($15 after dilution). Scenarios of a price of $20k at 34% peak share or a $25k price but only 20% peak market share both indicate $5 per share before any funding. However, this ignores any other indications or the value of a successful cell therapy to an established company. Cephalon's deal with Mesoblast was $130m upfront, a $220m equity investment and up to $1.7bn in milestones.

Sensitivities

Aastrom offers high upside given the growing CLI market and solid Phase IIb data released so far. The clinical risk lies in the use of the harder amputation-free survival endpoint in Phase III, which was only indirectly tested in Phase IIb. The use of a more ill patient group makes events more likely, but raises the therapeutic hurdle that ixmyelocel-T has to achieve. To achieve $1bn+ revenue, ixmyelocel-T needs to show enough amputation-free survival improvement to establish a $25,000 price point with at least 33% of eligible patients treated. The Termuo (Harvest) device could enter the market, which could disrupt the market for cultured cells and might limit it to severe cases. The ischaemic dilative cardiomyopathy indication has only interim, anecdotal data so far.

Financials

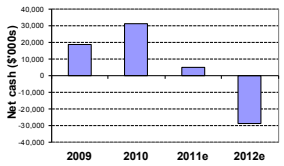
Aastrom's Q2 SEC filing shows an annualised burn rate of $25m (based on $12.6m in H1); this has risen from $17m in calendar 2010, possibly due to costs attached to the impending CLI Phase III study. Cash on 30 June was $18.5m after the net $20.6m equity funding in December 2010. A new funding round will be needed, possibly after starting the CLI Phase III and ideally after publishing RESTORE final data to enable a full evaluation of Phase III prospects.

Exhibit 7 Financial model

Note: The year-end changed from June to December in 2010. Hence, a transitional six month 10-K was filed with the SEC and is used here in historic accounts. The current financial year runs from January to December 2011. Interim data to June 2011 has been reported. Aastrom did a $21.6m equity fund-raising (net $20.6m) in December 2010.

$'000s	2010	2010t	2011e	2012e
	Year to June	Six mths to Dec		
31-December	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	**89**	**253**	**18**	**18**
Cost of Sales	0	(2)	(4)	(4)
Gross Profit	89	251	14	14
EBITDA	**(17,212)**	**(11,364)**	**(26,942)**	**(33,000)**
Operating Profit (before amort. and except.)	**(17,804)**	**(11,623)**	**(27,534)**	**(33,592)**
Intangible Amortisation	0	0	0	0
Exceptionals	3,171	(7,500)	(1,210)	0
Other	0	0	0	0
Operating Profit	**(14,633)**	**(19,123)**	**(28,744)**	**(33,592)**
Net Interest	75	35	64	40
Profit Before Tax (norm)	**(17,729)**	**(11,588)**	**(27,470)**	**(33,552)**
Profit Before Tax (FRS 3)	**(14,558)**	**(19,088)**	**(28,680)**	**(33,552)**
Tax	0	0	0	0
Profit After Tax (norm)	**(17,729)**	**(11,588)**	**(27,470)**	**(33,552)**
Profit After Tax (FRS 3)	**(14,558)**	**(19,088)**	**(28,680)**	**(33,552)**
Average Number of Shares Outstanding (m)	24.7	29.2	38.6	38.6
EPS - normalised (c)	(71.7)	(39.7)	(71.1)	(86.9)
EPS - normalised and fully diluted (c)	(71.7)	(39.7)	(71.1)	(86.9)
EPS - (IFRS) (c)	(58.9)	(65.4)	(74.3)	(86.9)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	99.2	78.0	78.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	**1,013**	**1,128**	**1,660**	**1,668**
Intangible Assets	0	0	0	0
Tangible Assets	1,013	1,128	1,660	1,668
Investments	0	0	0	0
Current Assets	**19,518**	**31,699**	**4,894**	**1,654**
Stocks	0	0	0	0
Debtors	16	25	0	0
Cash	19,119	31,248	4,894	1,654
Other	383	426	0	0
Current Liabilities	**(2,661)**	**(3,910)**	**(3,255)**	**(3,603)**
Creditors	(2,435)	(3,696)	(3,152)	(3,500)
Short term borrowings	(226)	(214)	(103)	(103)
Long Term Liabilities	**(3,089)**	**(25,995)**	**(27,192)**	**(57,164)**
Long term borrowings	(79)	(41)	(28)	(30,000)
Other long term liabilities	(3,010)	(25,954)	(27,164)	(27,164)
Net Assets	**14,781**	**2,922**	**(23,893)**	**(57,445)**
CASH FLOW				
Operating Cash Flow	**(15,085)**	**(9,252)**	**(25,711)**	**(32,652)**
Net Interest	73	35	64	40
Tax	0	0	0	0
Capex	(120)	(305)	(600)	(600)
Acquisitions/disposals	0	0	0	0
Financing	17,324	21,686	17	0
Dividends	0	0	0	0
Net Cash Flow	2,192	12,164	(26,230)	(33,212)
Opening net debt/(cash)	**(16,622)**	**(18,814)**	**(30,993)**	**(4,763)**
HP finance leases initiated	0	0	0	0
Other	0	15	0	0
Closing net debt/(cash)	**(18,814)**	**(30,993)**	**(4,763)**	**28,449**

Source: Company historic accounts, Edison estimates

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 08-12e	N/A	ROCE 11e	N/A	Gearing 11e	N/A	Address:	
EPS CAGR 10-12e	N/A	Avg ROCE 08-12e	N/A	Interest cover 11e	N/A	24 Frank Lloyd Wright Drive, Lobby K Ann Arbor, MI 48105	
EBITDA CAGR 08-11e	N/A	ROE 11e	N/A	CA/CL 11e	N/A		
EBITDA CAGR 10-12e	N/A	Gross margin 11e	N/A	Stock turn 11e	N/A	Phone	(734) 418-4400
Sales CAGR 08-12e	N/A	Operating margin 11e	N/A	Debtor days 11e	N/A	Fax	(734) 665-0485
Sales CAGR 10-12e	N/A	Gr mgn / Op mgn 11e	N/A	Creditor days 11e	N/A	www.aastrom.com	

Principal shareholders (as of 30 June 2011)	%
BlackRock	5.0
Vanguard	1.8
Mindshare	1.2
Fuller & Thaler	0.7
Geode	0.5

Forthcoming announcements/catalysts	Date *
RESTORE clinical data	Nov 2011
Q3 2011 10-Q	Nov 2011
2011 10-K	Mar 2012
Q1 2012 10-Q	May 2012
Q2 2012 10-Q	Jun 2012
*Note: * = estimated*	

Management team

CEO: Timothy M Mayleben

Tim joined Aastrom in June 2005. Previously, he was with ElMa Advisors. He has been President of NightHawk Radiology and COO of Esperion (acquired by Pfizer in 2004). He holds an MBA from the Kellogg School of Management.

CSO: Dr Ronnda L Bartel

Ronnda joined Aastrom in 2006 becoming CSO in 2010. She was a director at Microlslet and a VP at StemCells Inc. She worked at Advanced Tissue Sciences and at SRS Capital. Ronnda has a PhD from the U of Kansas.

VP Clinical and Regulatory: Sharon Watling

Sharon joined Aastrom in 2010. Previously, she was with Cognigen Corporation and has held senior clinical development positions at Metabasis and Pfizer. Sharon holds a PharmD from the U of Michigan College of Pharmacy.

VP Finance: Brian Gibson

Brian joined Aastrom in 2010 becoming VP Finance in October 2011. Previously, he was a senior manager at PricewaterhouseCoopers. He holds a BA in accounting from Michigan State University and is a certified public accountant.

Companies named in this report

Pluristem Therapeutics (PSTI), Apceth, Temuro, Pfizer (PFE), Abbott Laboratories (ABT), CR Bard, Harvest Technologies, Arteriocyte