EDISON

Athersys

Fresh finance secured

Opportunity knocks in 2014

Pharma & biotech

Athersys has raised $18.7m (net) from the sale of 5m shares at $4.10 after a c 100% share price surge in the past month. This follows an $18.5m (net) equity raise in December. We estimate a current cash balance of $51m, providing Athersys with enhanced financial flexibility as it seeks to fully exploit the potential inherent in MultiStem, its allogeneic stem cell product. This includes the prospect of accelerated development/approval in Japan; we now include this in our valuation, which rises to $370m or $4.85 per share (vs $222m/$3.15 per share). This is ahead of Phase II data in 2014, in ulcerative colitis and ischaemic stroke, which could re-rate the stock.

Year end	Revenue ($m)	PBT* ($m)	EPS* ($)	DPS ($)	P/E (x)	Yield (%)
12/11	10.3	(14.6)	(0.63)	0.0	N/A	N/A
12/12	8.7	(17.1)	(0.53)	0.0	N/A	N/A
12/13e	2.4	(24.0)	(0.42)	0.0	N/A	N/A
12/14e	4.9	(20.9)	(0.27)	0.0	N/A	N/A

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

Further shareholder support

As with the December issue, all participating investors were existing shareholders of the company. The offering also included 1.5m stock-equivalent warrants at a $4.50 strike price, which are immediately exercisable and expire in July 2016. Athersys now has approximately 10.4m in stock-equivalent warrants and 7.8m stock options outstanding.

On track for a pivotal year

Enrolment into the Phase II ulcerative colitis (UC) study, being conducted by long-term partner Pfizer, was completed in December, and headline efficacy results (change in endoscopic score at week 8) are expected in April/May. Recruitment into the Phase II trial in ischaemic stroke continues, with the recent addition of UK sites to boost enrolment in H114. Initial results should be available in H214. Positive results from either study, but particularly stroke, could significantly re-rate the stock.

A unique opportunity in Japan

Athersys has been granted three new patents in Japan related to the composition and therapeutic applications of its MultiStem product. We previously highlighted new legislation in Japan designed to accelerate the development and approval of regenerative medicines, although we had not specifically included this opportunity in our valuation. With $51m in cash, and the option to draw on a $25m Aspire Capital equity facility, we have added the development of MultiStem in Japan to our model and look forward to further regulatory/commercial developments in 2014.

Valuation: Increased to $370m, or $4.85 per share

We have increased our sum-of-the-parts DCF model to $370m, or $4.85 per share (vs $222m/$3.15 per share), after including the $18.7m (net) equity raise and risk-adjusted estimates for MultiStem's potential to reach the market for stroke in Japan (150,000 annual incidence) and Europe (800,000). We note this is fair value for the shares ahead of the key clinical trial catalysts for MultiStem in 2014.

Athersys is a research client of Edison Investment Research Limited

21 January 2014

Price	**US$4.05**
Market cap	**US$309m**
Net cash ($m) at Q413e	32.0
Shares in issue	76.3m (post 5m share issue)
Free float	96%
Code	ATHX
Primary exchange	NASDAQ
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	86.6	128.8	224.0
Rel (local)	89.5	109.8	161.0

52-week high/low: US$4.0 / US$1.2

Business description

Athersys is a US biotechnology company focused on developing MultiStem (allogeneic stem cells) for a range of indications. Phase II studies are ongoing in ulcerative colitis and ischaemic stroke. A 5HT2c agonist programme (obesity/schizophrenia) is available for partnering.

Next events

Ulcerative colitis Phase II data	April/May 2014
Stroke Phase II data	H214
Start AMI Phase II study	Mid-2014
5HT2c agonist programme partnerships	2013/14

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Athersys data sheet

Exhibit 1: Athersys's product pipeline

Product	Indication	Status	Next milestones	Notes
MultiStem	Inflammatory bowel disease (ulcerative colitis; Crohn's disease)	126-pt Phase II study in UC	Apr/May14: headline results	In development under 2009 Pfizer collaboration ($6m upfront). Up to $105m milestones + royalties receivable.
MultiStem	Ischaemic stroke	140-pt Phase II study	Q214: complete enrolment H214: headline results	27 US sites, adding six sites in the UK, potential in RoW. Partner(s) sought post Phase II data.
MultiStem	Acute myocardial infarction	Phase II-ready	Mid-2014: start Phase II (prep-work ongoing)	Aug 2013: $2.8m SBIR fast track grant awarded for Phase II study; prep-work for study underway.
MultiStem	Graft vs host disease/ organ transplantation	Phase II/III planned for GvHD 12-pt Phase I ongoing in liver transplant	Q114: resubmit GvHD Phase II/III study protocol to FDA H114: FDA feedback on GvHD protocol 2015: liver transplant study results	A pivotal Phase II/III study protocol for GvHD will be re-submitted to the FDA in Q114, following FDA feedback (May 2013) on previous protocol submission (end-2012). Phase II/III start dependent on securing a partner and/or fresh finance. Liver transplant Phase I study ongoing in Germany.
MultiStem	Multiple further uses, including: traumatic brain injury, multiple sclerosis, spinal cord injury	Preclinical		Completed various pre-clinical studies in models of MS, TBI and SCI, funded by research grants.
5HT2c agonist programme	Obesity/schizophrenia	Preclinical	Seeking development partner(s)	Developed 5HT2c agonist specific compounds (lack activity at 5HT2b/a = safer), with partner(s) sought for clinical development.
MAPC technology	Orthopaedic implants	Aug 2013: First human implantation of graft in spinal surgery	End-2013: launch map3 cellular allogeneic bone graft	In development through 2010 RTI Surgical collaboration ($5m upfront) – RTI fully responsible, with milestones + royalties receivable.
RAGE technology	Human cell line for drug targets, to enable compound screening and development	Rolling BMS deal		Bristol-Myers Squibb collaboration in 2000 provides BMS with access to RAGE technology for internal drug development programmes. Athersys receives licence fees, development milestones and royalties on approved products. At Dec 2012, $9.7m licence fees and $1.8m milestones had been received to date.

Source: Company reports and presentations

Exhibit 2: Phase II trial design in ulcerative colitis

Aim	Assess the safety and possible clinical benefit of MultiStem in adult patients with moderate-to-severe UC
Summary design	International (US, Canada, Europe), randomised, double-blind, placebo-controlled, parallel group, 16-week study
Design details	128 pts; 18+ yrs; active moderate-to-severe UC (Mayo score >6 and Baron score ≥2 in previous 7 days) and failed/intolerant to at least one of oral corticosteroids/azathioprine or 6-MP/anti-TNFs. After low (300m cells)/high (750m cells) dose cohorts (n=9), in Cohort 3 (n=88 evaluable patients), 1:1 randomisation to placebo or MultiStem as IV infusion on day 1. At week 8, all patients receive additional dose of MultiStem or placebo, with 50% treatment cross-over = 22 patients receive second MultiStem dose, 22 patients receive second placebo dose, 44 patients cross-over to alternative treatment (placebo/MultiStem) from day 1.
Primary endpoints	Incidence and severity of AEs at weeks 4, 8, 12 and 16; change from baseline in modified Baron endoscopic score at week 8; change from baseline in Mayo rectal bleeding sub-score at weeks 4 and 8.
Secondary endpoints	Multiple assessments, including: change in total Mayo score at week 8; % clinical remission at week 8 (Mayo ≤2, no individual sub-score >1); change in Mayo rectal bleeding sub-score at weeks 12 and 16.
Start date	Feb 2011
Completion dates	Jan 2014 (final data collection date for primary outcome measure); Apr/May 2014 (headline data); Oct 2014 (study completion date)

Source: Edison Investment Research; clinicaltrials.gov

Exhibit 3: Phase II trial design for ischaemic stroke

Aim	To examine the safety and potential effectiveness of MultiStem in adults who have suffered an ischaemic stroke
Summary design	US and UK, randomised, double-blind, placebo-controlled, parallel group, 90-day study
Design details	140 pts; 18-83 yrs; diagnosis of moderate-to-severe ischaemic stroke (8-20 NIHSS; mRS 3-5), occurring in last 24-48 hrs. After low (400m cells)/high (1.2bn) dose cohorts, Cohort 3 will use the highest safe dose, 1:1 randomisation to placebo or MultiStem as single IV infusion 24-48 hrs following ischaemic stroke.
Primary endpoints	Dose limiting AEs after seven days; % of subjects with a modified Rankin Scale (mRS) score ≤2 after 90 days.
Secondary endpoints	Multiple assessments, including: % subjects with excellent functional outcome (mRS = 0 to 1; NIHSS = 0 to 1; Barthel Index = ≥95) after 90 days; Total change in mRS scores after 90 days; frequency of AEs after 1 year.
Start date	Oct 2011
Completion dates	Jun 2014 (final data collection date for primary outcome measure); H214 (headline data); Mar 2015 (study completion date)

Source: Edison Investment Research; clinicaltrials.gov

Update: UC trial fully enrolled, data April/May

On 19 December 2013, Athersys announced that enrolment into the 128-patient study of MultiStem in patients with moderate-to-severe ulcerative colitis had been completed. Pfizer, a partner since 2009 for inflammatory bowel diseases (IBD), is conducting the trial and positive results resulting in advancement of the product into a pivotal Phase III programme would trigger milestone payments to Athersys – we assume $2.5m on positive Phase II data and $5m on starting a Phase III trial.

Full details of the study are displayed in Exhibit 2. The primary endpoints are safety (incidence and severity of adverse events over 16 weeks) and efficacy (change from baseline in modified Baron endoscopic score at week 8). Initial results based on efficacy/safety data after eight weeks (after a single IV infusion of MultiStem on day 1) are expected to be announced in April or May 2014. Further data for patients through 16 weeks (after an additional dose of MultiStem/placebo at week 8) will be released by the end of Q214, most likely in June. At week 8, 50% of patients will cross-over to MultiStem or placebo (opposite to day 1 dose), 25% will receive a second dose of MultiStem, and the final 25% will receive an additional placebo infusion. The trial design should provide reasonable insight into MultiStem's mechanism of action and potential for treating IBD.

For reference, we show the Baron and Mayo scoring scales and criteria in Exhibits 4 and 5. Changes from baseline in these scores are widely used clinical trial endpoints for assessing the effectiveness of therapeutics, and are accepted by the FDA to approve new agents for UC.

Exhibit 4: Modified Baron score for UC

Score	Criteria
0	Normal, smooth, glistening mucosa with vascular pattern visible; not friable
1	Granular mucosa; vascular pattern not visible; not friable; hyperemia
2	As 1, with a friable mucosa but not spontaneously bleeding
3	As 2, but mucosa spontaneously bleeding
4	As 3, but clear ulceration, denuded mucosa

Source: Edison Investment Research

Exhibit 5: Mayo Clinic score for UC

A	Stool pattern	Patient reports a normal number of daily stools = 0
		1-2 more stools than normal = +1
		3-4 more stools than normal = +2
		5 or more stools than usual = +3
B	Most severe rectal bleeding of the day	none = 0
		Blood streaks seen in the stool less than half the time = +1
		Blood in most stools = +2
		Pure blood passed = +3
C	Endoscopic findings	Normal or inactive colitis seen = 0
		Mild colitis: mild friability, erythema, decrease in vascularity = +1
		Moderate colitis: friability, marked erythema, vascular pattern absent, erosions seen = +2
		Severe colitis: ulcerations and spontaneous bleeding = +3
D	Global assessment by physician	Normal = 0
		Mild colitis = +1
		Moderate colitis = +2
		Severe colitis = +3
	Mayo Score range	**0 (no UC) to 12 (severe UC)**

Source: Edison Investment Research

The primary efficacy endpoint will also assess changes in the Mayo rectal bleeding sub-score at weeks 4 and 8. Secondary endpoints include a clinical remission rate at week 8, defined as patients with a Mayo score ≤2 and no individual sub-score >1. For reference, Takeda's vedolizumab (anti-α4β7 integrin MAb), which is expected to be approved by the FDA in 2014, achieved clinical remission rates after six weeks of 30-37% vs placebo (14-21%) in two Phase II studies.[1]

1 McLean L, et al. 2012. Vedolizumab for the treatment of ulcerative colitis and Crohn's disease. Immunotherapy. 2012 September; 4(9): 883–898.

Update: Accelerated framework in Japan

Japan's parliament recently enacted new legislation to enable the safe and accelerated development of stem cell-based therapeutics. The new laws define products containing stem cells as regenerative medicine and would allow the conditional approval of such products if safety has been confirmed in clinical trials, even if efficacy has not been fully demonstrated.

It is therefore possible that just one well conducted study (in a relatively small number of patients to determine a 'probable' efficacy benefit) would be required to gain provisional approval in Japan. Further studies and post-market surveillance would be requested for final approval, but a stem cell product could reach the market in three years, rather than six to 10 years currently.

Athersys continues to evaluate the potential development of MultiStem in Japan, and will inevitably need to secure partners to assist with the process. We anticipate further regulatory and commercial developments in 2014.

The recently issued patents in Japan are therefore important in laying the groundwork for further development. Patent #5,398,941 covers non-embryonic, multipotent stem cells, such as MultiStem, and applies to all therapeutic applications. Patent #5,399,709 covers the use of such stem cell therapies for the treatment of immune dysfunctions, such as graft-versus-host disease (GvHD), and inflammatory diseases and autoimmune disorders (eg IBD). The third patent covers the treatment of brain injuries, such as stroke and traumatic brain injury, with these multipotent stem cells.

Valuation

We have increased our sum-of-the-parts DCF model to $370m, or $4.85 per share (vs $222m/$3.15 per share). Our model, which applies a standard 12.5% discount rate, now includes an estimated $51m in current cash, after the $18.7m new equity issue is added to estimated end-December 2013 net cash of $32m. The other significant change in our valuation model (Exhibit 6) is the addition of MultiStem's potential to reach the markets in Japan and Europe for ischaemic stroke, where the annual incidence rates are estimated at 150,000 and 800,000 respectively. Maintaining the same probability of success (20%), market penetration (12.5%) and treatment price ($20,000), this increases the peak sales potential to $3bn, from $1.4bn previously in the US alone.

Exhibit 6: Athersys valuation and model inputs and assumptions

Value driver	rNPV ($m)	rNPV per share ($)	Prob. of success	Market launch	Peak sales	Royalty estimate	Patent expiry	Key assumptions
MultiStem in ulcerative colitis (US + EU)	55	0.72	35%	2018	$500m	8%-10%	2030	1.7m UC patients in US and EU; 10% addressable market (moderate-to-severe and refractory to available treatments); $15,000 effective annual cost of treatment; 6 years to peak sales; risk-adjusted milestones from Pfizer included ($2.5m on Phase II, $7.5m on successful Phase III, $25m on FDA approval)
MultiStem in ischaemic stroke (US, EU + Japan)	255	3.34	20%	2017	$3.0bn	15%	2030	Annual incidence of stroke in US (800,000) + EU (800,000) + Japan (150,000); 15% mortality rate; 85% ischaemic stroke; $20,000 effective annual cost of treatment; 6 years to peak sales
MultiStem in AMI (US)	99	1.29	25%	2020	$1.4bn	15%	2030	700,000 annual incidence of AMI in US; 15% mortality rate; 75% receive PCI; $20,000 effective annual cost of treatment; 6 years to peak sales
MultiStem in GvHD (US)	8	0.10	35%	2017	$50m	15%	2030	25,000 allogeneic HSCTs in the US (projected rate); 50% develop GvHD; 50% refractory to steroids; $15,000 effective annual cost of treatment; 6 years to peak sales
R&D	-54	-0.70						
Admin	-17	-0.23						
Tax	-26	-0.34						
Cash	51	0.66						$32m net cash at Q413e + $18.7m (net) from 5m share sale
Valuation	**370**	**4.85**						Based on 76.3m shares outstanding

Source: Edison Investment Research

Given the accelerated development and approval pathway in Japan, we now estimate MultiStem could reach the market in Japan by the end of 2017 (estimates for US and EU launches remain in 2018). Offsetting the higher valuation component for MultiStem in stroke is an increase in longer-term R&D expenses required to support development in Japan. We await more specific updates on clinical and licensing progress in 2014.

We note that Edison's valuation, which represents upside to Athersys' current market capitalisation of $309m and share price of $4.05, is not a price target, but the fair value at which we believe the stock should now be trading, ahead of upcoming catalysts, particularly the Phase II trial results in UC (Q214) and stroke (H214).

By way of illustrating the potential uplift in valuation resulting from positive clinical data and further development of MultiStem in UC and stroke, we show the impact in Exhibit 7 from passing clinical and regulatory milestones over the next few years.

Exhibit 7: Valuation scenario analysis

MultiStem opportunity	Scenario	Time of event	Prob. of success	Market launch	Peak sales	Royalty estimate	rNPV ($m)	rNPV per share ($)
Ulcerative colitis	Current (pre-Phase II data)		35%	2018	$510m	8%-10%	55	0.72
	Positive Phase II data	Q214	50%				+24	+0.31
	Pfizer advance into Phase III	H115	65%				+24	+0.31
	Positive Phase III data	H217	90%				+39	+0.52
	FDA + EU approval	H218	100%				+16	+0.21
	Potential uplift						**+103**	**1.35**
	Total end value						**158**	**2.07**
Ischaemic stroke	Current (pre-Phase II data)		20%	2017	$3bn	15%	255	3.34
	Positive Phase II data	H214	40%				+255	+3.34
	Secure partner and start Phase III	H115	55%				+191	+2.51
	Positive Phase III data	H217	85%				+383	+5.01
	FDA + EU approval	H218	100%				+191	+2.51
	Potential uplift						**+1,020**	**13.37**
	Total end value						**1,275**	**16.71**

Source: Edison Investment Research

This scenario analysis is based on adjusting the various risk assessments based on a future event but discounted back to January 2014 values. The aim is to gain an impression of how future events might affect the indicative fair value. Note that there is no guarantee that such events will occur and the market, regulatory and competitive frameworks will also change over time. Dilution from any future share issues is not taken into account.

Sensitivities

Athersys is subject to the risks typically associated with biotech company drug development, including the possibility of unfavourable outcomes in clinical trials and regulatory reviews, success of competitors and commercial decisions by partners or potential partners.

Specifically, the outcomes of MultiStem's Phase II studies in UC (Q214) and stroke (H214) are particularly important to determining the product's next development steps and commercial potential. Positive clinical data would offer the opportunity of fresh (non-dilutive) finance from new partnerships. Negative or inconclusive data would raise doubts about MultiStem's viability in these specific indications, and could have a negative read-across to other potential uses. The track record of R&D in stroke is poor so this is a particularly high-risk indication, although MultiStem's mechanism and dosing in a wider therapeutic window than conventional drugs could address prior challenges.

The Phase II studies in UC and stroke are not directly supported by prior clinical data specifically in these indications, which adds an element of risk. Both Phase II studies have also taken longer to

recruit than initially expected, which adds uncertainty over the completion of the stroke study and the potential timeframes for pivotal studies in these indications. We have made assumptions on market launch, cost of treatment and commercial uptake, which are likely to be subject to change on the basis of clinical trial outcomes and available finance.

Financials

We estimate that Athersys now holds approximately $51m in cash, after the $18.7m in net proceeds ($20.5m gross) from the new equity issue is added to estimated end-December 2013 net cash of $32m. The recent financings have significantly enhanced the company's financial flexibility and removed the near-term financing overhang that was present when we initiated coverage in October 2013. We estimate that current funds are sufficient into 2016, without the need to draw down on the $25m Aspire Capital equity facility, which expires in November 2015. We had previously assumed an $8m draw down on this facility in 2015, which we now remove from our financial model.

Athersys now has approximately 10.4m in stock-equivalent warrants and 7.8m stock options outstanding. A number of these warrants are now 'in-the-money' (3.95m at $1.01; 3.5m at $2.50; 1.31m at $3.55), and a number may have been exercised in recent months given the share price gains. However, per Edison policy, we do not include assumptions in our financial and valuation models that these are exercised. Our financial model is summarised in Exhibit 8.

Exhibit 8: Financial summary

$'000s	2011	2012	2013e	2014e	2015e
Year end 31 December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS					
Revenue	10,344	8,708	2,368	4,900	6,800
Cost of Sales	0	0	0	0	0
Gross Profit	10,344	8,708	2,368	4,900	6,800
Research and development	(18,930)	(19,636)	(20,072)	(19,163)	(19,738)
Selling, general & administrative	(4,916)	(4,753)	(6,012)	(6,192)	(6,378)
EBITDA	(14,921)	(17,493)	(24,380)	(21,265)	(20,125)
Operating Profit (before GW and except.)	(14,643)	(17,173)	(24,038)	(20,861)	(19,721)
Intangible Amortisation	0	0	0	0	0
Exceptionals/Other	0	0	0	0	0
Operating Profit	(14,643)	(17,173)	(24,038)	(20,861)	(19,721)
Net Interest	85	34	9	0	0
Other (change in fair value of warrants)	812	2,404	(2,353)	0	0
Profit Before Tax (norm)	(14,558)	(17,139)	(24,029)	(20,861)	(19,721)
Profit Before Tax (FRS 3)	(13,746)	(14,735)	(26,382)	(20,861)	(19,721)
Tax	0	0	0	0	0
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(14,558)	(17,139)	(24,029)	(20,861)	(19,721)
Profit After Tax (FRS 3)	(13,746)	(14,735)	(26,382)	(20,861)	(19,721)
Average Number of Shares Outstanding (m)	23.2	32.6	56.7	76.2	77.8
EPS - normalised ($)	(0.63)	(0.53)	(0.42)	(0.27)	(0.25)
EPS - FRS 3 ($)	(0.59)	(0.45)	(0.47)	(0.27)	(0.25)
Dividend per share ($)	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET					
Fixed Assets	1,267	1,294	1,324	1,300	1,287
Intangible Assets	0	0	0	0	0
Tangible Assets	1,267	1,294	1,324	1,300	1,287
Other	0	0	0	0	0
Current Assets	14,434	26,309	32,878	32,076	13,771
Stocks	0	0	0	0	0
Debtors	689	490	453	453	453
Cash	12,784	25,533	32,142	31,340	13,035
Other	961	286	283	283	283
Current Liabilities	(7,420)	(4,478)	(4,447)	(4,447)	(4,447)
Creditors	(7,420)	(4,478)	(4,447)	(4,447)	(4,447)
Short term borrowings	0	0	0	0	0
Long Term Liabilities	(983)	(2,878)	(4,841)	(4,841)	(4,841)
Long term borrowings	0	(169)	(174)	(174)	(174)
Other long term liabilities	(983)	(2,709)	(4,667)	(4,667)	(4,667)
Net Assets	7,298	20,247	24,914	24,089	5,770
CASH FLOW					
Operating Cash Flow	(14,489)	(17,665)	(22,401)	(19,120)	(17,914)
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(590)	(347)	(372)	(381)	(391)
Acquisitions/disposals	0	0	0	0	0
Financing	12,595	30,357	29,382	18,700	0
Dividends	0	0	0	0	0
Other	0	0	0	0	0
Net Cash Flow	(2,484)	12,345	6,609	(802)	(18,305)
Opening net debt/(cash)	(15,181)	(12,784)	(25,364)	(31,968)	(31,166)
Exchange rate movements	0	0	0	0	0
Other	87	235	(5)	0	0
Closing net debt/(cash)	(12,784)	(25,364)	(31,968)	(31,166)	(12,861)

Source: Athersys accounts, Edison Investment Research. Note: We have removed our previous assumption that Athersys draws on the $25m Aspire Capital equity agreement in 2015.

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