e-Therapeutics plc

Four clinical trials in progress; new drug candidates in laboratory testing

Significant step change made in the productivity of the discovery process

16 September 2014: e-Therapeutics plc (AIM: ETX), the drug discovery and development company, today announces its half year results for the six months ended 31 July 2014.

Operational highlights

Cancer trials for lead cancer drug ETS2101 continue

- Phase I trials ongoing for UK and US studies in a variety of solid tumours and brain cancer
- Primary endpoint of Phase Ia trials met; drug is well tolerated at concentrations likely to be effective and update to market expected in Q4 2014
- Well advanced in the design of the phase Ib/II study, initially in hepatocellular and pancreatic cancers
- Phase I study of oral form starting the fifth cohort of healthy volunteers; completion expected Q4 2014

Progress on other programmes – ETS6103 and ETX1153c

- Phase IIb trial of ETS6103 in major depressive disorder expanded to enrol an additional c.140 patients; unblinding of the trial expected in H2 2015
- ETX1153c against *C.difficile* – actively looking for external funding to enable resumption of development

Accelerated rate of drug analysis by Network Pharmacology Discovery platform

- Approx. 1,000 molecules across three discovery projects being tested *in vitro* (FY2014: c.100 molecules)
- Processing speeds now 20 times faster than two years ago
- Significant step change in productivity of discovery process

Financial highlights

- Cash and liquid resources remain strong at £37.0 million at 31 July 2014 (31 January 2014: £43.1 million)
- Hall year loss before tax of £5.3 million (six months to 31 July 2014: loss of £3.1 million) as spend increased in both Discovery and Development activities
- During the period, appointment of new Finance Director, Steve Medlicott and plans for the Chairman, Professor Oliver James to retire at the end of 2014

Professor Malcolm Young, CEO of e-Therapeutics, said:

“As our clinical programmes continue apace in four current clinical trials, a further key change for the Company in the period has been the tangible acceleration in processing speeds and productivity of our Discovery platform based on network pharmacology. Over the past two years, we have been fortunate to receive significant funding to invest in the discovery engine. We are now seeing the results of this investment, from network analysis processing speeds that are 20 times faster to a greatly enhanced database of protein interaction and compound bioactivity data. We will select the most promising compounds and expect them to enter preclinical development by the end of H2 2015 to enter the clinic in 2017.

“Professor James has indicated that he will retire at the end of 2014. On behalf of the Company, I would like thank Oliver for his long and sterling service to the Company, and wish him a pleasant retirement. A further announcement about succession will be made in due course.

“e-Therapeutics is in a strong position to deliver shareholder value as it capitalises on fully functioning drug discovery and clinical development programmes with a strong balance sheet. We look forward to providing further updates in the short term on our development programmes and in the medium term on our discovery activities.”

-Ends-

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e-Therapeutics plc

Overview

e-Therapeutics' strategy is to discover and develop promising drug compounds for out-licensing, with a focus on age-related diseases including cancer and central nervous system disorders.

Our drug discovery process is based on network pharmacology, an area that we pioneered in the early 2000s and one that is backed by a strong patent portfolio. Network pharmacology considers the biocomplexity of diseases and uses network science and chemical biology to identify compounds that have multiple optimised intervention points within a cellular disease network.

The discovery platform itself has been strongly developed over the last two years, and so far in 2014 it has identified approximately 1,000 molecules that are being evaluated *in vitro*. In drug development, we have two compounds undergoing clinical testing: ETS2101 is in phase I trials for various forms of cancer, and ETS6103 is in a phase IIb trial for major depressive disorder. Our clinical research partners are currently running a total of four clinical trials in the UK and US. We expect to report results from the current ETS2101 trials by the end of the current financial year.

Clinical highlights

ETS2101 - cancer trials continue

Our phase I programme for ETS2101 includes a UK trial for solid tumours, a US trial in brain cancer, and an oral bioavailability study. All the trials have a dose-escalating design with the primary objective being to demonstrate the safety and tolerability of the drug.

In the UK solid tumour trial, we have enrolled 31 patients so far, including nine at the current dose level of 30 mg/kg. There have been two hypersensitivity events at this dose level, but the investigators consider that these were not dose-limiting events. In addition, one patient left the current cohort due to a non-drug-related serious adverse event. At the current dose level, some patients experienced temporary side-effects, including a feeling of significant light-headedness and in some cases mild tremor.

At the current dose level, we have seen drug concentrations in circulating plasma that are at a level that we believe relates *in vivo* with those that were highly effective in killing cancer cells in the laboratory. These pharmacokinetic (PK) data indicate that the primary objective of this phase Ia study to demonstrate safety and tolerability of ETS2101 at doses likely to be effective has been met. Exploration of dose escalation and of alternative ways to give the infused doseform is continuing. We expect to be able to update the market more fully on the current UK trial in Q4 2014. We are well advanced in our design of the phase Ib/II study and will move rapidly into this phase at the appropriate time.

The US brain cancer trial is ongoing and has enrolled 18 patients in six cohorts to date, including three at the current dosage of 28 mg/kg; two patients remain on study. There have been no serious adverse events in this trial although the patients have experienced similar short-term side effects to those observed in the UK trial. Dose escalation is continuing. We anticipate reporting preliminary results on the current cohort in Q4 2014.

The phase I oral dosing study is being carried out in the UK. It is a dose-escalating study, looking at PK levels and bioavailability of ETS2101 in this form. We are currently starting the fifth cohort, each consisting of six active and two placebo doses in healthy volunteers. Completion of the trial is expected by the end of the current year.

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ETS6103 patient recruitment extended

ETS6103 is aimed at major depressive disorder. The phase IIb trial commenced late last year is designed to evaluate ETS6103 as a second-line therapy for patients who have not responded adequately to first-line treatment (of a selective serotonin reuptake inhibitor, or SSRI). The aim of the study is to establish whether ETS6103 has non-inferior antidepressant activity to that of amitriptyline.

The trial is a randomised double-blind controlled study and is being conducted in a group of primary care centres in Glasgow. The initial plan was to enrol 250 patients with expectations that around 160 patients who had not responded adequately to the first-line treatment would be randomised and enter the double blind controlled study. To date we have screened 170 patients and randomised 65. The investigators have experienced both a better than expected response to the first-line treatment and have also reported that 12 patients have left the trial before completion of the randomised treatment. We now believe that we will need to enrol around 140 additional patients to reach the aim of randomising 160 to the double blind controlled study.

Consequently, there has been a modest increase in the cost of the trial, and unblinding is now expected in H2 2015 rather than H1 2015. If the results are positive we would then aim to seek to out-license the drug.

ETX1153c - funding opportunities are being explored

ETX1153c is active against Clostridium difficile (*C. difficile*). It combines two constituents, miconazole and nisin. Extensive testing suggests that it is very hard indeed for the bacteria to generate any resistance to the drug, and pathogenic strains that are resistant to existing antibiotics do not show resistance to ETX1153c. Last year we decided to halt unilateral development due to cost and the likely small market size. The need for new antibiotics has been widely discussed globally by both policy makers and the science community over the last six months. We continue to believe that ETX1153c potentially offers an attractive opportunity in this area, and we are actively looking at potential external funding opportunities that would enable resumption of development on a commercially viable basis.

Discovery platform - higher rate of drug analysis

Discovery has seen a dramatic acceleration of molecule testing in the first half of the year with approximately 1,000 molecules, across three discovery projects, being tested *in vitro.* This compares to about 100 molecules that were tested in the previous year. Each of these tested molecules has a network pharmacology rationale as good as or better than that of each of our current clinical development assets, as our discovery processes have improved since ETS2101 and ETS6103 were discovered.

This improvement in productivity has been made possible by major developments and improvement of our discovery platform over the last two years. For instance we have made advancements both in our network analysis processing speeds and internal database coverage of protein interaction and compound bioactivity data. The platform's computer processing speeds are now 20 times faster than two years ago. In practice, this means that the computational analysis of a disease process that could have taken up to six months in the past can now be completed in just over a week. Our chemo-proteomic database size has also increased by a factor of four and our protein interaction database by an order of magnitude over the same period.

As we enter H2 2014, we expect a further three discovery projects to undergo analysis and aim to have many more molecules being tested *in vitro.* By the end of the next financial year, we intend to have analysed up to 10 discovery projects and to have undertaken *in vitro* testing of many thousand molecules, each with a strong rationale from network pharmacology. We aim to select the most promising of the compounds from the discovery process to enter pre-IND development and pre-clinical testing by the end of H2 2015, and intend that the most promising of these will enter clinical development in 2017.

Increased investment is supported by a strong balance sheet

The Group's first half operating loss was £5.3 million (six months to 31 July 2013: loss of £3.1 million), as spend increased in both the Discovery and Development activities within the business. Net interest receivable was £0.2 million (six months to 31 July 2013: £0.3 million) reflecting both a lower average cash balance and a slightly lower interest rate. The increased spend in the period means that the anticipated R&D tax credit for the period was £1.0 million (six months to 31 July 2013: £0.5 million) resulting in a post-tax loss of £4.1 million (six months to 31 July 2013: loss of £2.3 million).

The Group's cash balance at the end of July 2014 remained strong at £37.0 million. This was a £6.1 million reduction from the January 2014 year-end level of £43.1 million and compares to the operating loss of £5.3 million. The difference between the cash reduction and operating loss relates to an increase in prepayments within working capital offset slightly by interest received. At the end of the period we had unclaimed VAT of £0.3 million and since the half year end we have received an R&D Tax Credit refund in respect of the year ended 31 January 2014 for £1.1 million. We anticipate a similar cash outflow in the second half.

Outlook

The Group looks forward to reporting results from the current ETS2101 trials towards the end of the current year and expects to move rapidly into phase Ib/II trials shortly thereafter. In Discovery, the rate of compound testing has increased considerably, under a systematic selection process that is intended to yield clinical development candidates of the highest quality. The Group's strong balance sheet means that we continue to be confident that e-Therapeutics is fully funded into early 2019.

Finally, having served as Chairman for the last seven years, I have informed the Board of my intention to retire at the end of the current year. I am proud to leave a fully funded group that has exceeded my early hopes and one that is in a very exciting period of its development.

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GROUP INCOME STATEMENT

FOR THE SIX MONTHS ENDED 31 JULY 2014

	6 months ended 31 July 2014 (un-audited) £000	6 months ended 31 July 2013 (un-audited) £000	12 months ended 31 January 2014 (audited) £000
Revenue	**-**	-	-
Cost of sales	**-**	-	-
Gross profit	**-**	**-**	**-**
Research & Development expenditure	**(4,403)**	(2,550)	(5,367)
Administrative expenses	**(921)**	(540)	(1,352)
Operating loss	**(5,324)**	(3,090)	(6,719)
Financial income	**189**	306	617
Financial expenses	**-**	-	-
Loss before taxation	**(5,135)**	(2,784)	(6,102)
Taxation	**1,006**	503	1,063
Loss for the period	**(4,129)**	(2,281)	(5,039)
Loss per share - basic and diluted	**(1.56)p**	(0.93)p	(1.98)p

The results shown above relate entirely to continuing operations. There are no recognised gains and losses other than those passing through the income statement.

GROUP STATEMENT OF COMPREHENSIVE INCOME

FOR THE SIX MONTHS ENDED 31 JULY 2014

	6 months ended 31 July 2014 (un-audited) £000	6 months ended 31 July 2013 (un-audited) £000	12 months ended 31 January 2014 (audited) £000
Loss for the period	**(4,129)**	(2,281)	(5,039)
Other comprehensive income	**-**	-	-
Total comprehensive income for the period	**(4,129)**	(2,281)	(5,039)

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GROUP BALANCE SHEET
AT 31 JULY 2014

	Notes	31 July 2014 (un-audited) £000	31 July 2013 (un-audited) £000	31 January 2014 (audited) £000
ASSETS				
Non-current assets				
Property, plant and equipment		**106**	130	121
Goodwill		**-**	-	-
Intangible assets	2	**529**	458	496
		635	588	617
Current assets				
Tax receivable		**2,083**	1,348	1,077
Trade and other receivables		**1,938**	588	780
Fixed-term deposits		**28,000**	41,000	36,250
Cash and cash equivalents		**9,022**	4,364	6,897
		41,043	47,300	45,004
Total assets		**41,678**	47,888	45,621
LIABILITIES				
Current liabilities				
Trade and other payables		**1,116**	584	1,003
		1,116	584	1,003
Total liabilities		**1,116**	584	1,003
Net assets		**40,562**	47,304	44,618
EQUITY				
Share capital	3	**264**	264	264
Share premium	3	**64,528**	64,439	64,483
Warrant reserve	3	**-**	132	132
Retained earnings	3	**(24,230)**	(17,531)	(20,261)
Total equity attributable to equity holders	3	**40,562**	47,304	44,618

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GROUP CASH FLOW STATEMENT
FOR THE SIX MONTHS ENDED 31 JULY 2014

	6 months ended 31 July 2014 (un-audited) £000	6 months ended 31 July 2013 (un-audited) £000	12 months ended 31 January 2014 (audited) £000
Cash flows from operating activities			
Loss for the period	**(4,129)**	(2,281)	(5,039)
Adjustments for:			
Depreciation, amortisation and impairment	**35**	37	83
Loss on disposal of fixed assets		-	-
Financial income	**(189)**	(306)	(617)
Financial expenses	**-**	-	-
Equity-settled share-based payment expenses	**28**	7	35
Taxation	**(1,006)**	(503)	(1,063)
	(5,261)	(3,046)	(6,601)
Increase in trade and other receivables	**(1,485)**	(65)	(64)
Increase / (decrease) in trade and other payables	**109**	(296)	115
Tax received	**-**	-	830
Net cash from operating activities	**(6,637)**	(3,407)	(5,720)
Cash flows from investing activities			
Interest received	**521**	103	222
Acquisition of property, plant and equipment	**(14)**	(5)	(22)
Acquisition of other intangible assets	**(40)**	(92)	(150)
Decrease / (increase) in fixed-term deposits	**8,250**	(35,450)	(30,700)
Net cash from investing activities	**8,717**	(35,444)	(30,650)
Cash flows from financing activities			
Net proceeds from issue of share capital	**45**	38,990	39,042
Net cash from financing activities	**45**	38,990	39,042
Net increase in cash and cash equivalents	**2,125**	139	2,672
Cash and cash equivalents at the beginning of the period	**6,897**	4,225	4,225
Cash and cash equivalents at the end of the period	**9,022**	4,364	6,897

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GROUP STATEMENT OF CHANGES IN EQUITY
FOR THE SIX MONTHS ENDED 31 JULY 2014

	Share capital £000	Share premium £000	Warrant reserve £000	Retained Earnings £000	Total £000
As at 1 February 2013	138	25,567	132	(15,257)	10,580
Total comprehensive income for the period					
Loss for the period	-	-	-	(2,281)	(2,281)
Total comprehensive income for the period	-	-	-	(2,281)	(2,281)
Transactions with owners, recorded directly in equity					
Issue of ordinary shares	126	38,872	-	-	38,998
Equity-settled share-based payment transactions	-	-	-	7	7
Total contributions by and distribution to owners	126	38,872	-	7	39,005
As at 31 July 2013	**264**	**64,439**	**132**	**(17,531)**	**47,304**
As at 1 August 2013	264	64,439	132	(17,531)	47,304
Total comprehensive income for the period					
Loss for the period	-	-	-	(2,758)	(2,758)
Total comprehensive income for the period	-	-	-	(2,758)	(2,758)
Transactions with owners, recorded directly in equity					
Issue of ordinary shares	-	44	-	-	44
Equity-settled share-based payment transactions	-	-	-	28	28
Total contributions by and distribution to owners	-	44	-	28	72
As at 31 January 2014	**264**	**64,483**	**132**	**(20,261)**	**44,618**
As at 1 February 2014	264	64,483	132	(20,261)	44,618
Total comprehensive income for the period					
Loss for the period	-	-	-	(4,129)	(4,129)
Total comprehensive income for the period	-	-	-	(4,129)	(4,129)
Transactions with owners, recorded directly in equity					
Issue of ordinary shares	-	45	-	-	45
Lapse of warrants	-	-	(132)	132	-
Equity-settled share-based payment transactions	-	-	-	28	28
Total contributions by and distribution to owners	-	45	(132)	160	73
As at 31 July 2014	**264**	**64,528**	**-**	**(24,230)**	**40,562**

Notes

1. Basis of Preparation

These unaudited interim financial statements do not comprise statutory accounts as defined within section 434 of the Companies Act 2006. The Company is a public limited company; it is listed on the London Stock Exchange's AIM market and is incorporated and domiciled in the United Kingdom. The address of its registered office is 17 Blenheim Office Park, Long Hanborough, Oxfordshire, OX29 8LN, UK.

Statutory accounts for the year ended 31 January 2014 were approved by the Board of Directors on 23 May 2014 and delivered to the Registrar of Companies. The report of the Auditor on the accounts was unqualified, did not contain an emphasis of matter paragraph and did not contain any statement under section 498 of the Companies Act 2006.

This interim statement, which is neither audited nor reviewed, has been prepared in accordance with the measurement and recognition criteria of Adopted IFRSs. It does not include all the information required for the full annual financial statements, and should be read in conjunction with the financial statements of the Group as at and for the year ended 31 January 2014. It does not comply with International Accounting Standard (IAS) 34 'Interim Financial Reporting' as is permissible under the rules of AIM. The accounting policies applied in preparing these interim financial statements are the same as those applied in the preparation of the annual financial statements for the year ended 31 January 2014 (as defined therein) other than standards, amendments and interpretations which became effective after 1 February 2014 and were adopted by the Group. These have had no significant impact on the Group's result for the period or its equity.

2. Intangible Assets

Group

	Patents and trademarks	**Total**
	£000	**£000**
Cost		
Balance as at 1 February 2013	**706**	706
Other acquisitions - internally developed	**92**	92
Balance as at 31 July 2013	**798**	798
Other acquisitions - internally developed	**58**	58
Balance as at 31 January 2014	**856**	856
Other acquisitions - internally developed	**40**	40
Balance as at 31 July 2014	**896**	896
Amortisation and impairment		
Balance as at 1 February 2013	**328**	328
Amortisation	**12**	12
Balance as at 31 Jul 2013	**340**	340
Amortisation	**20**	20
Balance as at 31 January 2014	**360**	360
Amortisation	**7**	7
Balance as at 31 July 2014	**367**	367
Net book value		
As at 31 July 2013	**458**	458
As at 31 January 2014	**496**	496
As at 31 July 2014	**529**	529

3. Capital and Reserves

Reconciliation of movement in capital and reserves
Group

	Share capital £000	Share premium £000	Warrant reserve £000	Retained earnings £000	Total equity £000
As at 1 February 2013	138	25,567	132	(15,257)	10,580
Total recognised income and expense	-	-	-	(2,281)	(2,281)
Issue of ordinary share capital	126	38,872	-	-	38,998
Equity-settled share-based payments	-	-	-	7	7
Balance at 31 July 2013	**264**	**64,439**	**132**	**(17,531)**	**47,304**
Balance at 1 August 2013	264	64,439	132	(17,531)	47,304
Total recognised income and expense	-	-	-	(2,758)	(2,758)
Issue of ordinary share capital	-	44	-	-	44
Equity-settled share-based payments	-	-	-	28	28
Balance at 31 January 2014	**264**	**64,483**	**132**	**(20,261)**	**44,618**
Balance at 1 February 2014	264	64,483	132	(20,261)	44,618
Total recognised income and expense	-	-	-	(4,129)	(4,129)
Issue of ordinary share capital	-	45	-	-	45
Lapse of warrants	-	-	(132)	132	-
Equity-settled share-based payments	-	-	-	28	28
Balance at 31 July 2014	**264**	**64,528**	**-**	**(24,230)**	**40,562**

All 875,761 warrants outstanding at 31 January 2014 lapsed unexercised during March 2014.

Share capital

	31 July 2014 (un-audited) '000	31 July 2013 (un-audited) '000
In issue - fully paid		
Ordinary shares of £0.001 each	264,177	263,579
	£000	£000
Allotted, called up and fully paid		
Ordinary shares of £0.001 each	264	264
Shares classified as liabilities	-	-
Shares classified in shareholders' funds	264	264
	264	264

During the period, exercise of options over shares by former staff and issues of shares to Non-Executive Directors in part-payment of their fees led to an increase in share capital of £296 and a credit of £45,312 to the share premium account.