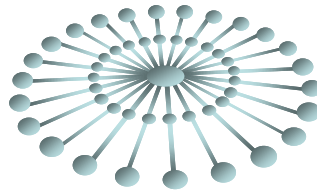
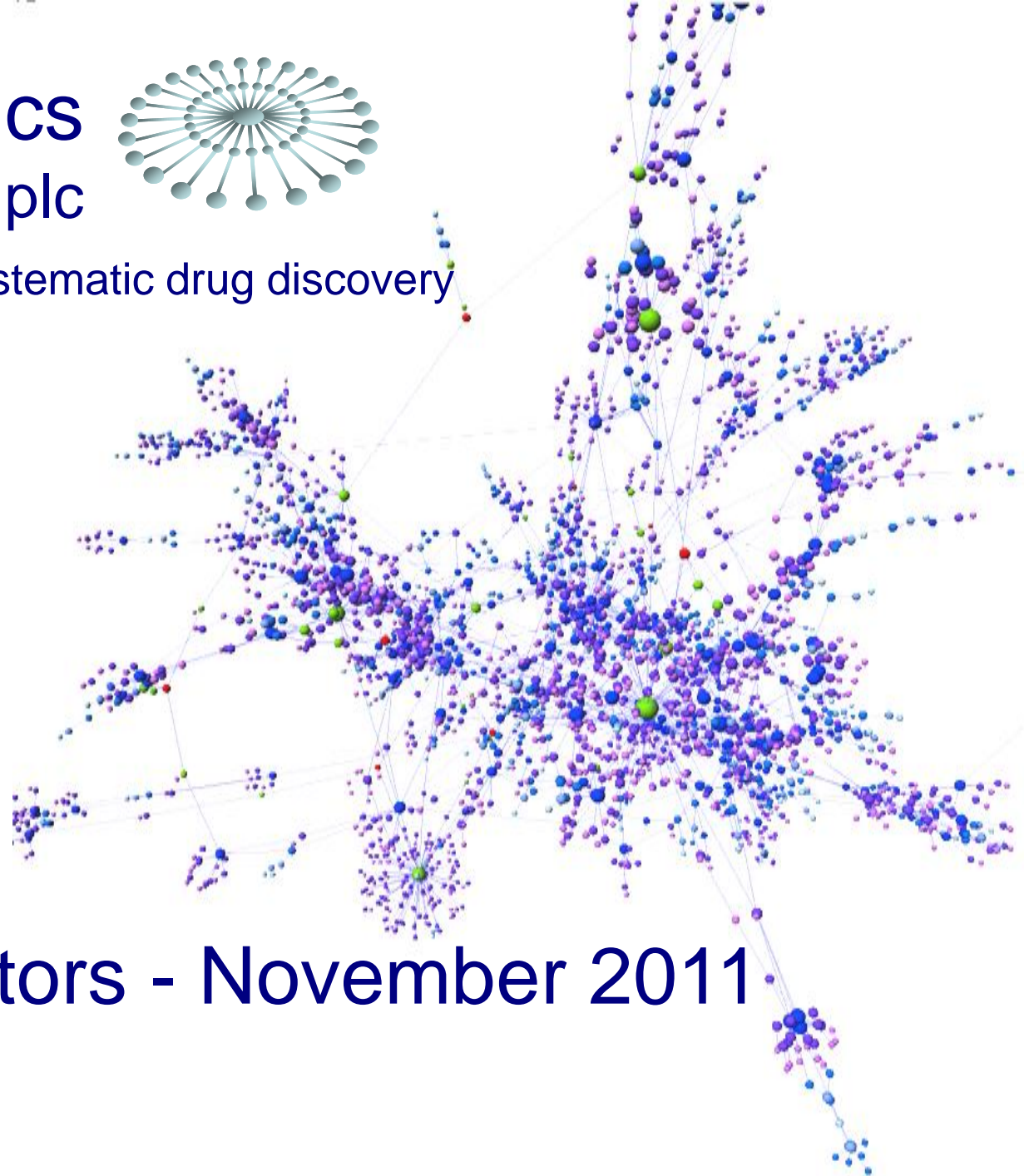


# e-Therapeutics plc



Systematic drug discovery



## Proactive Investors - November 2011

Dr Daniel Elger, CFO

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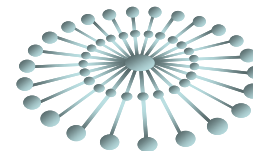
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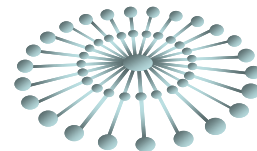
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# e-Therapeutics

- Drug discovery and development company
  - Platform technology in network pharmacology (NP)
  - Clinical pipeline of four drugs
  - Plan to realise value through partnering deals
- AIM-listed
- Raised £16.7 million in March 2011
- Cash of £15.3 million at 31 July 2011
- Major investors include Invesco (47%) & Henderson (11%)



# R&D investment and returns

## Discovery

- NP platform
- New Oxford centre
- One+ new drug by 2013
- *Up to £4m mid-'11 thru '13*

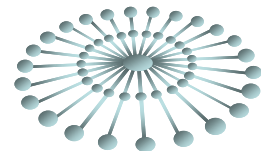


## Development

- Best 4 drugs into trials
- Trials start in 2012
- Significant data in 2012/13
- *Up to £10m mid-'11 thru '13*

Potential discovery collaborations

Product licensing deals



# Looking forward to 2012

## 2011

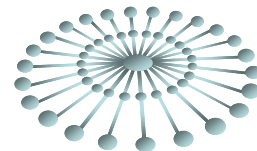
- Business recapitalised
- Restart of discovery: new hires and site
- Preparation for clinical trials

## 2012

- Discovery fully active
- Trial starts for 4 drugs
- First trial data
- Ramp-up of BD activity

**Increasing interest in NP approach**

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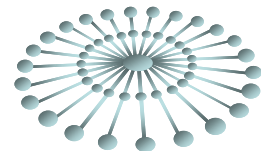
# Limitations of 'conventional' drug discovery

- Focus on one 'bad actor' driving disease (usually a protein)
- Aim to hit hard and specifically



6a

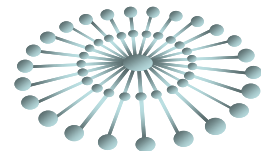
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# Limitations of 'conventional' drug discovery

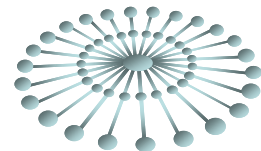
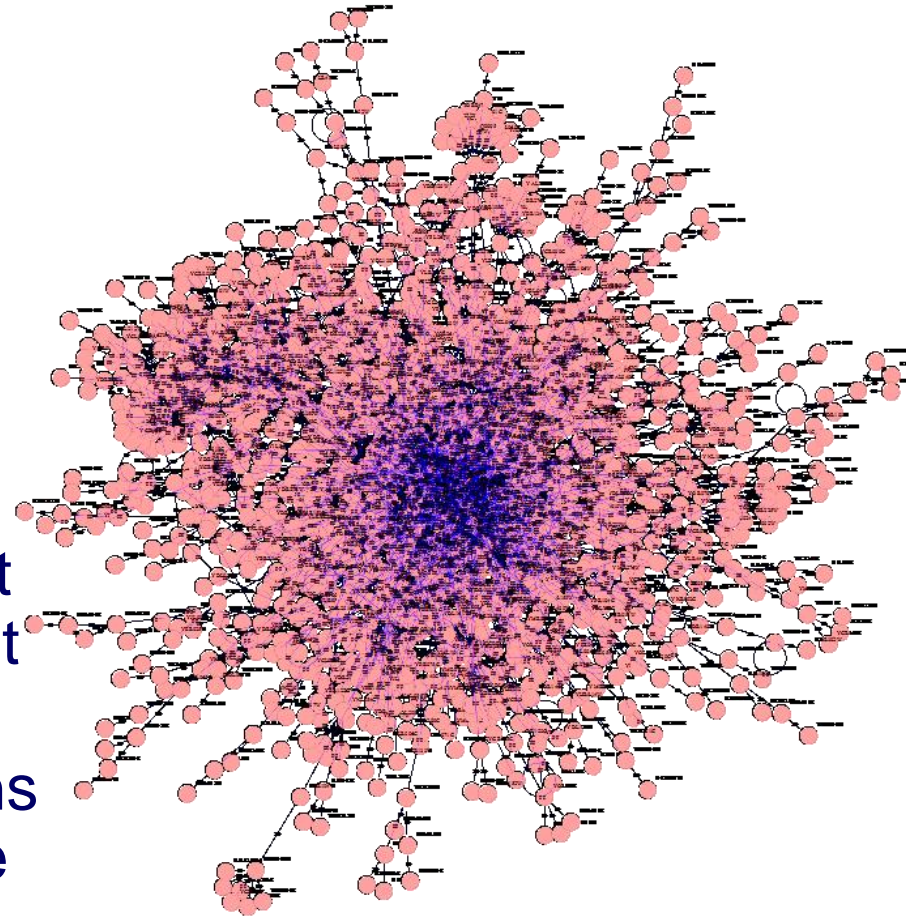


- But any drug will interact with multiple proteins
- Unplanned interactions will often be undesirable
- Some 'off-target' effects contribute to therapeutic benefit

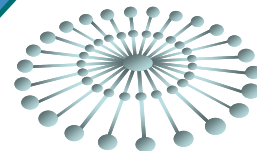
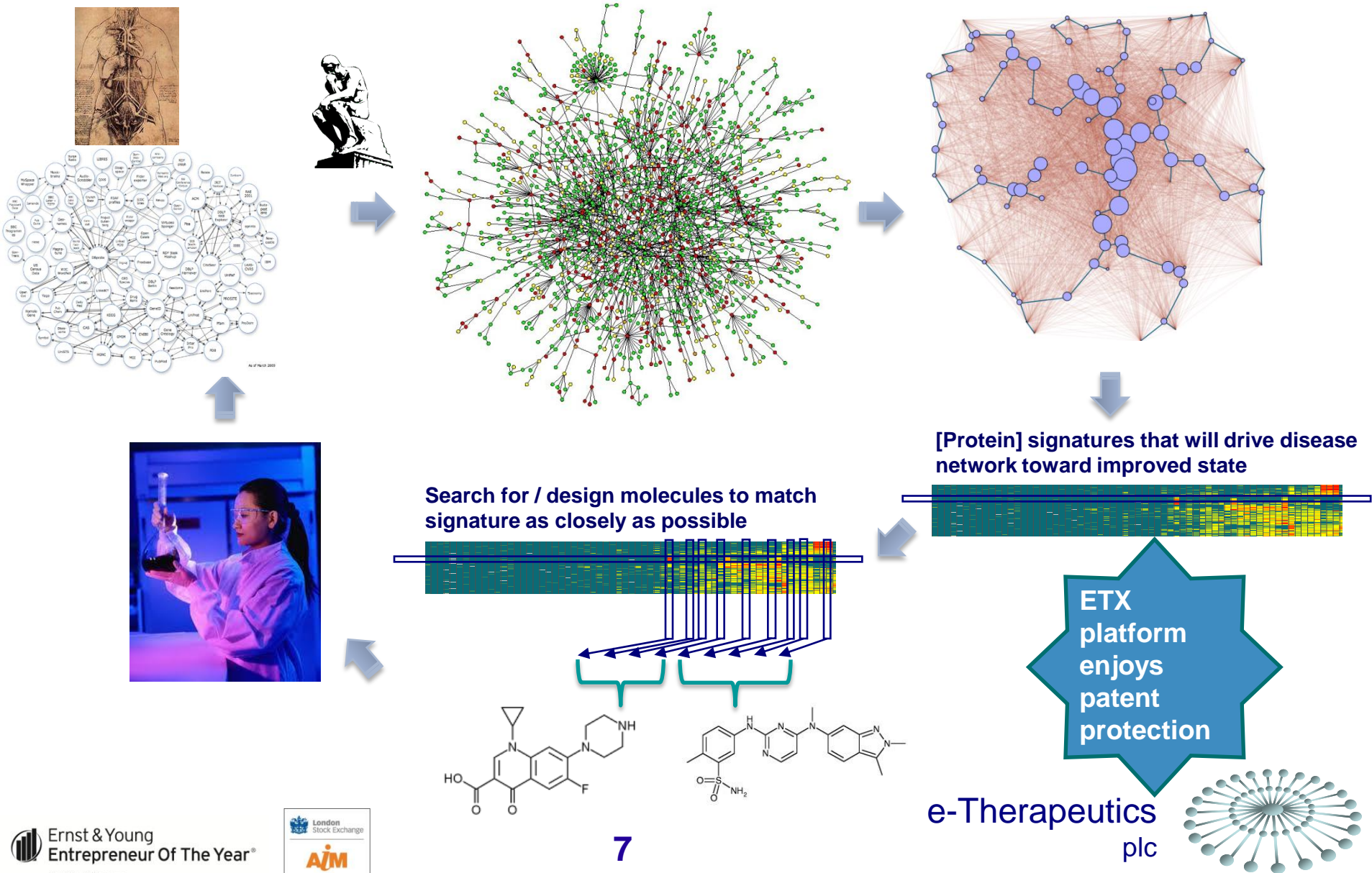


# Limitations of 'conventional' drug discovery

- Biological systems are a form of complex network
  - They have properties in common with other complex networks (the internet, an army)
  - They are highly robust against intervention at any single point
- We need multiple interventions at the right set of places in the network



# ETX's network pharmacology approach



# Application of the platform

## First wave of discovery (2005—2009)

- Focus on repositioning opportunities
- Four current clinical programmes resulted

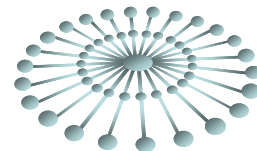
## New discovery programme 2011

- Concentration on two broad therapeutic areas
  - Cancer
  - Degenerative diseases of nervous system
- Both new and repositioning opportunities sought

Complex diseases – plays to strengths of NP approach

Major commercial opportunities

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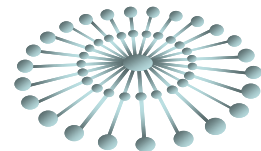


# Development strategy

Two key decisions taken in early 2011

- Focus on most promising development projects
  - 8 candidates → 4 lead candidates
  - Top priorities ETS2101 (cancer) & ETX1153c (*C. difficile*)
  - ETS6103 (depression) & ETX1153a (MRSA) also prioritised
- Shift trial investment to developed pharma markets
  - Longer timelines but higher quality data

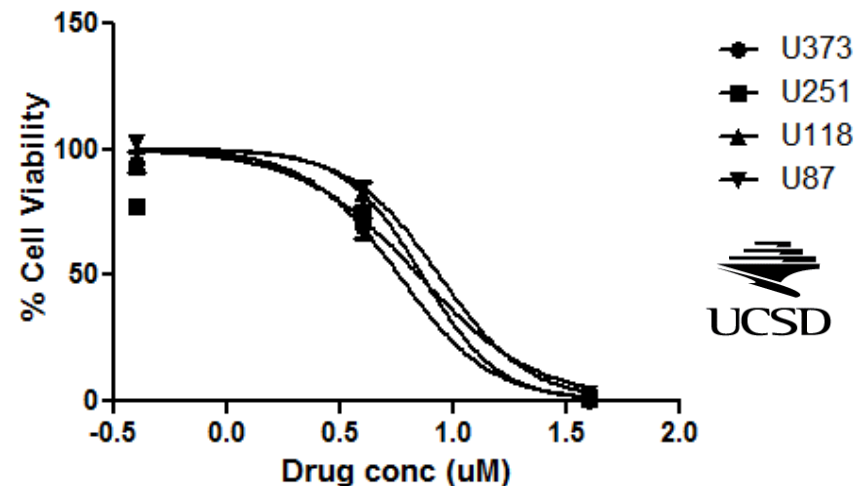
*Steve Self joined ETX to lead development in Dec 2010*



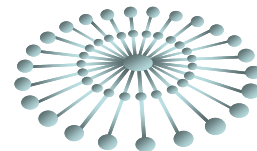
# ETS2101 – anticancer candidate

- Drug previously tested in trauma patients → phase III
  - Not effective but safe and well tolerated
- Platform indicated drug would promote apoptosis (programmed cell death)
  - Cancer cells rely on ability to avoid apoptosis
- Preclinical testing suggested broad anti-cancer activity
  - Particularly interesting results in brain cancer glioma

*Killing of four brain cancer cell lines by ETS2101*

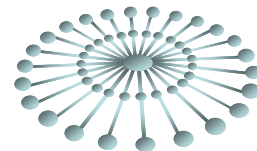


	U373	U251	U118	U87
IC50	5.766	7.063	7.287	8.678



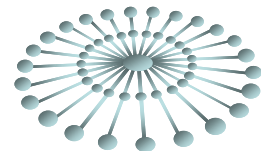
# ETS2101 – anticancer candidate

- Two parallel phase I trials to be conducted
  - #1 – patients with a variety of solid tumours
  - #2 – patients with brain cancers
- Both trials will explore dosing, safety and activity
- Both expected to start in early 2012
- Initial data expected 2012
- Final data expected 2013



# ETX1153c – anti-infective vs *C. difficile*

- *Clostridium difficile* causes life-threatening infections in hospitalised patients
- Targeting improved efficacy and lack of relapse compared to current brands
- NP platform identified miconazole + nisin as combination that would deliver strong antimicrobial effect
- Prediction supported *in vitro*
  - Combination effect clearly more than additive
  - ETX1153c effective even against drug-resistant strains
- Phase I to start early 2012; phase II to follow rapidly

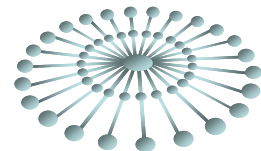


# ETS6103 – antidepressant candidate

- Tramadol for depression
- Encouraging data from small phase IIa trial vs amitriptyline
- Phase IIb dose-ranging trial to start early 2012; data H1 2013

# ETX1153a – topical anti-infective

- Combination of disulfiram and miconazole
- Topical therapy for MRSA – initially decolonising health workers
- Preclinical work ongoing; phase I to start 2012



# Significant market opportunities

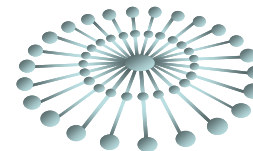
## Target product profile

## Analyst peak sales estimate

ETS2101 Oncology	Selective apoptotic against multiple cancers with favourable tolerability profile	\$300m (a)
ETX1153c <i>C.difficile</i>	Potent, fast-acting efficacy against <i>C.difficile</i> , including resistant strains, with low rate of recurrence	\$100m (b)
ETS6103 Depression	Fast-acting efficacy with low side-effects for patients who do not respond to SSRIs**	\$230m (c)
ETX1153a MRSA topical	Potent fast-acting efficacy against all MRSA strains, with a very low rate of resistance (topical)	\$100m (d)

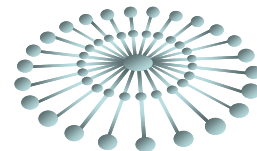
- (a) Panmure Gordon analyst note (glioblastoma only)
- (b) Panmure Gordon analyst note
- (c) Canaccord analyst note
- (d) Objective Capital analyst note

\*\* Selective serotonin reuptake inhibitors, commonly used anti-depressants



# Newsflow increasing

Programme	News	Expected
ETS2101	Regulatory discussions initiated with MHRA	DONE
ETS6103	Start of phase IIb trial in depression	Q1 2012
ETS2101	Start of phase I programme in cancer	Q1 2012
ETX1153c	Start of phase I trial in C. dif. Infections	Q1 2012
ETX1153a	Start of phase I trial – topical MRSA	Q3 2012
ETX1153c	Data from phase I trial (C. dif. infections)	Q4 2012
ETS2101	First interim findings from phase I programme	Q4 2012
ETS6103	Data from phase IIb trial in depression	H1 2013
ETS2101	Data from phase I solid tumour trial	2013
ETS2101	Data from phase I brain cancer trial	2013
ETX1153a	Data from phase I trial - topical MRSA	2013
ETX1153c	Start of phase II trial in C. dif. infections	H1 2013
ETX1153c	Data from phase II trial in C. dif. infections)	H2 2013
Discovery	At least one new drug → development	2013



# e-Therapeutics - summary

- Drug discovery and development company
  - NP technology platform plus clinical pipeline
  - Plan to realise value through pharma partnering deals
- Four drugs in / entering clinical development
- New wave of discovery activity recently started
- Well-funded: cash for existing programmes and new discovery
- Wealth of newsflow through 2012 and 2013

