

e-Therapeutics plc
("e-Therapeutics" or "the Company")

ETS2101 effective in *in vitro* studies against skin cancer and commences *in vivo* studies

e-Therapeutics plc (AIM: ETX), the systems biology drug discovery company, today announces the successful completion of *in vitro* testing of its drug candidate ETS2101 in melanoma (skin cancer), and its progression into *in vivo* development.

Malignant melanoma is the most aggressive skin cancer, responsible for the majority of skin cancer related deaths, estimated to be more than 48,000 a year worldwide. Despite many years of intensive research, the only effective cure is surgical removal of the primary tumour at an early stage. Current drug treatments have limited effect and carry significant toxicity and tolerance problems. e-Therapeutics is developing ETS2101 as a first-line treatment for this very serious cancer.

In vitro testing of the potency of ETS2101 was carried out by the Northern Institute for Cancer Research at Newcastle University, which is supported by Cancer Research UK. The same group will also be involved in *in vivo* testing.

ETS2101 cytotoxic against all human melanoma cell-lines tested

When tested against a variety of established human melanoma cell-lines, including those derived from melanoma metastases in other tissues, ETS2101 was profoundly cytotoxic to all the cell-lines tested at concentrations distributed about a mean of 14 μ M. The results were concentration-dependent, following a smooth relationship in all tested cell-lines.

ETS2101 induced cell death in metastatic melanoma cells rather than merely slowing growth

Disseminated metastatic melanomas are highly resistant to current drug therapies. However, ETS2101 did not just slow growth in metastasized cells but was profoundly

cytotoxic to these malignant cells, which are the principal cause of the morbidity of the disease. This observed cytotoxic effect in the metastatic cells in other tissue was very similar to that observed in primary malignant melanoma cells. This property of ETS2101 is highly desirable as the ability to kill distributed melanoma cells, after metastasis has taken place, is a necessary property for a first-line treatment for this type of aggressive cancer.

A novel cytotoxic agent with a potentially high therapeutic index

The concentrations at which ETS2101 exerts its anti-tumour effects *in vitro* are comparable to the plasma levels of ETS2101 that have already been shown to be safe and well-tolerated in several hundred patients. Thus, the cytotoxic action of ETS2101 appears to be highly selective, leaving normal cells and tissues largely unaffected, potentially yielding a drug with a high therapeutic index (where the effective dose is only a fraction of that which produces side-effects).

Rapid, concentration-dependent killing

Cell death in primary malignant and metastatic melanoma cells was as profound after exposure for one hour as when exposed for 24 hours, and for five days. Professor Herbie Newell, Professor of Cancer Therapeutics and Director of Scientific Research at the Northern Institute for Cancer Research, who oversaw the testing, said “The observation we have made is that the compound produces concentration-dependent, but time-independent, effects on cells. This is very unusual for a cancer drug, where in most cases the effects are time-dependent or concentration-times-time dependent.” ETS2101 is therefore potentially capable of yielding its effects from a short, perhaps outpatient, treatment visit. This would be an important advantage over existing chemotherapy agents, which normally involve sustained high dosing over a long period, with related toxic and very unpleasant side effects.

Other cancers targeted by the same compound

The cellular mechanisms targeted by ETS2101 are also present in other cancers. e-Therapeutics will seek to demonstrate comparable efficacy in these other cancers, which include breast, colon, ovarian, lymphoma and pancreatic cancers. Since the low toxicity of this molecule has already been demonstrated, e-Therapeutics believes that ETS2101 has high potential as a broad spectrum drug in cancer.

Dr Roy Drucker, Medical Director of e-Therapeutics, said: “We are very excited by the prospects for this compound, not only in melanoma, a very aggressive skin cancer, but also in several other serious cancers. In my experience, it is very unusual to see rapid and complete killing of metastatic cancer cells at a concentration that suggests such a low side-effect burden for the patient. If these promising results are borne out in the clinic, ETS2101 could become the future chemotherapeutic of choice in melanoma.”

Professor Malcolm Young, the e-Therapeutics CEO, added: “We have now started *in vivo* testing of this exciting candidate. For me, this is drug discovery at its most rewarding: ETS2101 showing efficacy in a disease that has been so difficult to address by conventional means shows the power of our systems biology platform to identify promising new treatments, even in the toughest areas.”

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e-Therapeutics plc is a systems biology drug discovery company. It has developed proprietary computational systems to swiftly and accurately analyse and predict how medicines interact with cells in the body. This optimises the probability of identifying drug candidates with desirable efficacy and low toxicity. The Company applies its novel, systematic approach to three areas of activity:

- discovery of new drugs;
- discovering novel uses for existing drugs; and
- analysis of the interactions between different drugs.

Amongst e-Therapeutics' pipeline of compounds in development are novel antibiotics that have been shown to kill the "superbug" MRSA, and candidate therapies targeted at atherosclerosis, asthma and depression. The Company is currently in negotiation with a number of pharmaceutical companies, and is progressing the preclinical and clinical development of these products.

For further information on e-Therapeutics visit www.etherapeutics.co.uk.

About *in vitro* and *in vivo* testing

In vitro testing involves testing of drug candidates in a laboratory medium, such as a cell culture. By contrast, *in vivo* testing involves testing within a living organism.