MorEx

MTL-005 Clinical Stage, Global Licensing Opportunity

- High Unmet Clinical Need
- Orphan Designation for Head & Neck Cancer
- Broad Potential Market
- Limited Competition

High Unmet Clinical Need

Radiotherapy is the mainstay of treatment for many cancer patients, yet tumours recur in around half of patients treated with the intent to cure. In addition, radiotherapy can cause side effects that may restrict the dose that patients are able to tolerate, since it non-selectively kills both healthy tissue and tumour cells.

> *"Radiotherapy still produces a high rate of local failure in spite of all the technologies. So, true radiation-modifying drugs or radiation-sensitizing drugs could have a huge market."*
>
> KOL interview.

Novel Radio-Enhancer Compound

MTL-005 is a boronated metalloporphyrin in development as a radio-enhancer: a drug given to patients prior to conventional radiotherapy or chemoradiotherapy and designed to amplify the effect of radiotherapy. It does not appear to be pharmacologically active and, as such, it is expected to have a good safety profile.

MTL-005 preferentially accumulates in tumour cells and interacts with the X-rays to generate reactive oxygen species that selectively kill the tumour cells. Evidence suggests that MTL-005 can enhance the effects of radiation regardless of the oxygen status of the target tumour.

Broad Clinical Utility

Once efficacy is proven with standard radiotherapy and also in combination with chemoradiotherapy regimens, the utility of MTL-005 may be expanded further to allow clinical oncologists to reduce the overall dose of radiotherapy given to a patient. If this becomes possible, in addition to reducing the side effects experienced by patients, MTL-005 could have additional pharmaco-economic benefits by allowing more efficient use of radiotherapy suites, with potentially higher throughput of treated patients.

Efficacy in Multiple Solid Tumour Types

More than half of current cancer patients have radiation therapy and it is a mainstay of treatment in head and neck, breast, lung, prostate, cervical, brain and pancreatic cancer. MTL-005 is initially being developed as an adjuvant for first-line radiotherapy in head and neck cancer but it is expected that it will also be effective in other solid tumours where radiotherapy is used.

There are pre-clinical data to support the use of MTL-005 in breast cancer, while studies with related metalloporphyrins suggest potential efficacy in lung, oesophageal, prostate, pancreatic, bladder, brain and cervical cancer.

Orphan Designation in Europe

MTL-005 was granted orphan designation in June 2013 for 'Treatment of squamous cell carcinoma of the head and neck in patients undergoing radiotherapy.' Once approved, MTL-005 will benefit from a 10-year market exclusivity period within the EU.

Ideal PK-PD Profile to Target Tumours

MTL-005 is the culmination of years of research by the original investigators at the internationally renowned Brookhaven National Laboratory in New York. Their original aim was to develop boron-delivery agents optimised for use with boron neutron capture therapy (BNCT). The team focussed on developing agents with low systemic toxicity and low uptake by normal tissues compared to tumour tissues, along with rapid clearance from the blood and normal tissue. An additional feature that they selected for was persistence within the tumour since this allows time for the therapy to be delivered.

During the development of their boronated metalloporphyrin series, it was discovered that the family of compounds to which MTL-005 belongs could be used with conventional radiotherapy rather then requiring specialised units with alternative neutron sources.

Limited Competition

True 'radio-enhancers' differ from 'radio-sensitisers'. With a radio-enhancer, the active drug moiety boosts the effects of the radiation and if, like MTL-005, the radio-enhancer selectively accumulates within the tumour cells, this amplification effect is focused within the tumour cells. MTL-005 is not pharmacologically active and, as such, it is expected to have a good safety profile.

Nimoral (nimorazole) is a hypoxic radio-enhancer that has been available under a compassionate use protocol for head and neck cancer in Denmark since 2011. However there are still no radio-enhancers approved for use in either the US or the wider EU.

The term radio-sensitiser is commonly used to describe drugs, such as cytotoxics, that are pharmacologically active and make cells more prone to damage by radiation. In many cases these agents act non-selectively and patients can experience significant side effects.

There are two oncology drugs that have approved indications as radio-sensitisers: temozolomide and cetuximab.

Simplifying Approach for Clinical / Radiation Oncologists

Several radio-sensitisers are being tested in the clinic, however, many of these approaches require combinations of cytotoxic drugs administered with patient-specific dosing regimens, the drugs themselves have side effects and, as is the case with molecularly-targeted drugs, they may only be effective in certain types of tumours. To make life even more complicated for clinical oncologists, the timing of administration of these drugs prior to radiotherapy can be critical and repeat doses are usually required if fractionated (spilt) doses of radiotherapy are being used.

MTL-005 should offer a more straightforward solution. It is expected that a single dose level will be used for all patients and that it can be administered up to a week before radiotherapy is scheduled. It is anticipated that MTL-005 will enhance radiotherapy treatment of a range of solid tumours and its longevity in tumour tissue means that a single dose could be used to cover an entire radiotherapy treatment plan.

First-in-Man Studies Underway

The UK MHRA has reviewed the pre-clinical safety data and has approved the first-in-human clinical study. The study was initiated in the first UK centre in mid-2013. By working with an established network of CMOs, CROs and KOLs, MorEx expects the first-stage of the study should complete by late-2014.

Clear Regulatory Pathway

Two metalloporphyrin-based, photo-sensitising agents (Photofrin® and Foscan®), have already been approved by the regulatory authorities in the US and EU (respectively). As a consequence, the regulators have knowledge and experience in the assessment of porphyrin-based new chemical entities such as MTL-005.

Stable Product with Long Shelf Life

The Drug Product is a kit comprising the Drug Substance plus two solvents used for reconstitution. The kit has initial shelf life of at least 27 months at room temperature.

Administration is via slow intravenous infusion, which can be given to the patient anywhere from 3 to 7 days prior to initiating the radiation treatment. A single dose of MTL-005 is expected to be sufficient for the duration of a multi-week course of radiotherapy.

Scalable Manufacturing Process

MTL-005 offers a scalable synthetic manufacturing process using well established manufacturing and analytical methods. This presents major advantages for reduced capital investment requirements. A competitive cost of goods offers pricing flexibility at attractive gross margins to a commercial partner.

Robust Intellectual Property Position

The MTL-005 programme has a robust intellectual property position. It is based on extensive, international patent applications comprising both composition-of-matter and methods-of-use claims. The base patent has been granted in the US and is in final filings in Europe. Methods-of-use and formulations patents have also been filed for international coverage and are currently under review. There should be international coverage on MTL-005 until at least mid-2030.

Clinical-Stage, Global Licensing Opportunity

MorEx's radio-enhancer programme represents a unique opportunity to enhance the efficacy of radiotherapy in the treatment of several solid tumours - an area of high unmet clinical need.

MorEx is seeking an experienced development and commercialisation partner to continue the MTL-005 programme.

Summary

Expected Benefits of MTL-005

For Patients	• Improved tumour control • Potential for reduced dosing and fewer side effects
For Clinicians	• Simple, flexible addition to existing radiotherapy/chemo-radiotherapy protocols • Single dose requirement for duration of radiotherapy/chemo-radiotherapy dosing schedule • Potential to improve efficiency of radiotherapy suite
For Licensee	• 10-year market exclusivity in lead, orphan indication • Opportunity to expand use to multiple tumour types

Ideal profile of a radio-enhancer

Uptake	• High uptake by tumour tissue • Low uptake by normal tissue
Toxicity	• Low systemic toxicity
Clearance	• Rapid clearance from blood • Persistence within tumour

MorEx

MorEx is a private business entirely focused on advancing MTL-005 through the clinic and into the product portfolio of a committed commercial partner. The company has a strong and experienced biopharma management team who work closely with leading clinical oncology experts.

For more information on MorEx, please visit www.morexdevelopments.com

For further information please contact:

Professor John Caldwell, Chairman of the Board:

john.caldwell@morexdevelopments.com

Chris Beattie, Development Director:

chris.beattie@morexdevelopments.com

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High Unmet Clinical Need

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Orphan Designation in Europe

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Efficacy in Multiple Solid Tumour Types

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Ideal PK-PD Profile to Target Tumours

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Simplifying Approach for Clinical Oncologists (Radiation Oncologists)

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