



1. Introduction

Unique worldwide, the private UK biotechnology company **PhotoBiotics** is focussing on **truly targeted photodynamic therapy (*t*-PDT) as a mainstream clinical reality**. Interest from PDT clinicians underlines PhotoBiotics' potential to address major unmet medical needs in cancer and other areas, while opening up new opportunities for early minimally invasive treatments.

Strong collaborations with two world-beating academic groups at Imperial College (IC), London (targeted therapeutics and photochemistry), mean PhotoBiotics confidently maintains its technological competitive edge (see the latest media news stories on the above web-site).

Photodynamic therapy (PDT) has recently emerged as a significant therapeutic modality, Novartis/QLT achieving worldwide sales for Visudyne (verteporfin) of around \$0.5billion for treatment of wet Age-related Macular Degeneration (AMD). Despite their effectiveness, all current photosensitisers suffer from very poor selectivity for their target tissues, significantly limiting PDT's commercial potential. PhotoBiotics *t*-PDT approach will vastly improve its own and current photosensitisers, thereby greatly expanding PDT's therapeutic use and commercial value.

2. Licensing Opportunity

PhotoBiotics' collaborations and business model mean its research resources are flexible. It has already achieved *in vivo* proof-of-concept, and recent equity investment. Thus, the company is now positioned to advance its research projects to significant value-enhancing milestones. Priority projects are to develop photo-immunoconjugates (PICs) for prostate cancer (ProstaLite™) and bladder cancer, as well as diagnostic applications of *t*-PDT.

Having demonstrated the flexibility of its coupling technology for other proprietary photosensitisers and antibodies, PhotoBiotics' targeted PDT platform will be extremely attractive to companies with complementary technologies, in particular those already in the PDT and antibody spaces. This summary document is provided to potential partners with a view to initiating further collaboration and licensing deals.

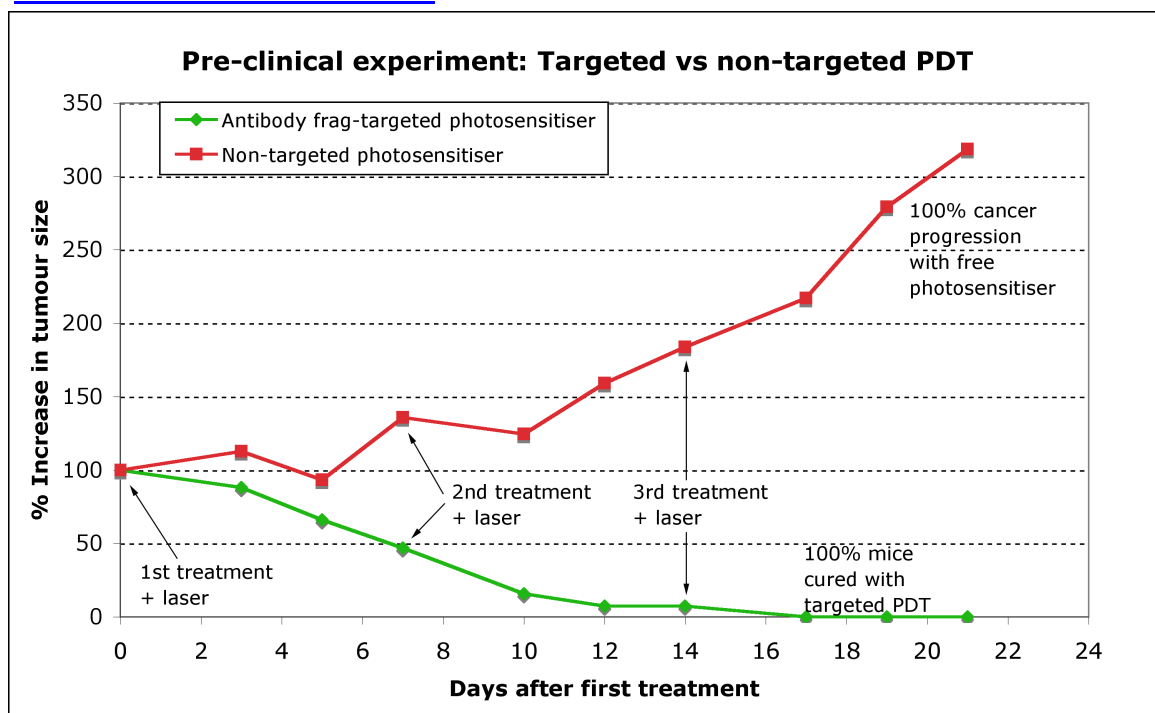
3. Proprietary Technology Platform I - PhotoLink™

Photobiotics has developed innovative, reliable, and patented coupling methods (PhotoLink™ technology platform) for attaching photosensitisers to relevant targeting antibody fragments (scFv), so creating therapeutic entities known as Photo-ImmunoConjugates (PICs).

Antibody fragment *t*-PDT promises to solve the crucial weaknesses of conventional PDT, which suffers from poor tissue selectivity and localization, resulting in proximal tissue damage and slow systemic clearance. Better localisation of the photosensitiser in target tissue will lead to greatly expanded indications and enhance ease of use for both the physician and the patient. PhotoBiotics' targeted PDT addresses these needs because it ensures:

- **High selectivity** of PICs toward cancer cells compared to free photosensitiser; almost zero phototoxicity against non-target cell lines; and excellent *in vitro* cell kill results.
- **Fewer side effects** anticipated because *in vivo* clearance is much improved over free photosensitiser, with improved blood clearance resulting in high therapeutic indices.
- **Selective targeting of tumours *in vivo***

- **Significant tumour regression and cure in animal models** when treated with PhotoLink™ PICs. (see, *The International Journal of Cancer* <http://www3.interscience.wiley.com/cgi-bin/fulltext/116837461/HTMLSTART>)



4. Proprietary Technology Platform II - Photosensitiser Innovation

PhotoBiotics' research has also led to considerable advances in the design of effective photosensitisers. Four patent-protected key innovations incorporate:

- **Porphyrin core modification:** enhances photophysics, leading to enhanced cell killing.
- **Triple bonds :** improve depth penetration of light into tissues.
- **Hydrophilic groups :** for ease of photosensitiser formulation and delivery.
- **A pre-designed single reactive group :** for ease of photosensitiser conjugation to scFvs

Additionally, PhotoBiotics' research on several PICs has demonstrated how fine-tuning certain photosensitiser features brings added benefits. Using various commercially available photosensitisers, PhotoBiotics has shown that its particular improvements to photosensitiser hydrophilicity *suppress:*

- ? **Aggregation and precipitation:** significant problems associated with water soluble dyes.
- ? **Non-covalent binding** of photosensitisers to scFvs during conjugation.

These significant improvements in photosensitiser manufacturing lead to increased reproducibility and yields of PICs, which retain all the excellent photophysical properties of the original photosensitiser molecules. In addition, our PIC technology vastly improves the LD₅₀'s of some commercially-available photosensitisers (see *Photochemical and Photobiological Sciences*, DOI:10.10391b708320c).

PhotoBiotics is currently incorporating all these innovations into a new patentable generation of photosensitiser derivatives readily produced through robust, commercially viable syntheses.

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