



SUPPORTING INNOVATION AND TECHNOLOGY TRANSFER IN ONCOLOGY

THERAPY

MMD

Mitochondrial Metabolism Disruptors for Therapeutic Intervention in Oncology



CONTEXT & BACKGROUND

The company is developing a new approach in the field of cancer metabolism to tackle cancer resistance and relapse. The approach targets mitochondrial function in cancer cells with a first-in-class Mitochondrial Metabolism Disruptors, NBS037. This novel, patent protected small molecule inhibits mitochondrial protein synthesis to selectively induce dysfunction in cancer-mitochondria; an effect that is anti-proliferative and sensitizing to Standard-of-Care agents. Using Patient Derived Xenograft tumors, from late stage, resistant, metastatic patients, The company was able to show single agent activity in OxPhos-dependent tumours (driven by the metabolic rewiring associated with a SMARCA4 loss of function mutation). Most importantly long-term antitumor efficacy was observed in combination with paclitaxel in a Non-Small Cell Lung OxPhos-dependent tumour model, and in combination with Sorafenib in a Clear Cell Renal Cell carcinoma. The candidate NBS037 is in preclinical development in preparation for Phase 1 in late stage patients failing current therapies.

Note : NBS037 has 2 back-up compounds with mitigated ADMET properties ; the company has also other chemical series in lead-optimisation stage.



INNOVATIVE COMPONENT & TECHNOLOGY

The fundamental design of the company's drug discovery approach is to create MMD compounds utilising its proprietary NoviChem platform consisting of a mitochondrial targeting group (MTG) joined by a non-cleavable linker to an antibiotic, all of which can be guided by in silico design and vary in nature and composition, thus creating novel chemical matter. The antibiotics selected are known to bind the mitochondrial ribosome and antagonise its function, thereby inhibiting mitochondrial protein synthesis in order to generate mitochondrial dysfunction.

KEYWORDS

Cancer metabolism,
Mitochondria, OXPHOS,
Treatment Resistance,
Relapse, Antibiotics



OBJECTIVES

The company is keen to secure a pharmaceutical partner that will bring additional resource and development capability to this innovative programme. We believe that this partnership will deliver novel therapeutics addressing primary and relapsed disease.



DEVELOPMENT & MATURATION STAGE

The company is open to licensing and collaborations. Its lead MMD NBS037 can be developed through preclinical and into the clinic by a pharma partner whilst the back-up compounds are further progressed. Alternatively, an investor may elect to invest in the company.



TARGET POPULATION

Human malignancies, solid and haematological, under 2 clinical settings, involving mitochondrial functional output reliance - a targetable vulnerability used as a liability from a therapeutic standpoint:

- 1) Metabolic tumour growth - predisposed under genetic determinants (oncogenic conditional behaviour). Related to bioenergetic (demonstrated - OXPHOS metabolism) and biosynthetic intermediates generated by the mitochondria
- 2) Chemoresistance & sensitisation of the SoC agent used (demonstrated) - resistance mechanisms OXPHOS-dependent.



TARGET PROFILE

The mitochondrion is at the heart of cellular metabolism and has been suggested over recent years as an attractive target within cancer cell populations from various cancer paradigms. The company's approach to eradicate such cancer cell populations aberrantly reliant upon an exacerbated mitochondrial output is based on leveraging the endosymbiotic theory, with the targeting of antibiotics to the mitochondria. The aim is to interfere with mitochondrial biogenesis and homeostasis, leading to mitochondrial dysfunction. To this end the company has developed several NCE series which selectively antagonise mitochondrial protein synthesis and eradicate tumour cells, including the most refractory.



STRENGTHS & COMPETITIVE ADVANTAGES

- Pre-Clinical Candidate, with potential to be First-in-Class Mitochondrial Metabolism Disruptor as a Cancer Therapeutic
- Tailored to impact on the treatment of patients with resistant tumours
- Potential for broad range of clinical indications
- Potential for low cost of goods - affordable cancer treatment
- Established Back-Up Programme
- Robust Patent Portfolio

In summary, with the right partner, opportunity for First-in-Man.



INDUSTRIAL APPLICATIONS & OPPORTUNITIES

The company's MMDs are suitable for late stage patients, in particular, patients demonstrating resistance and relapse, where few agents are effective. In addition, tumours with an OxPhos dependency are amenable. This is a growing area of interest to pharma. The market in the US is large with over 26m patients at risk of relapse from 2026 (ACS).



INTELLECTUAL PROPERTY & PATIENT CO-OWNER(S)

One patent owned by the company