Palladacycle - an Anti-Cancer Therapeutic

Offers reduced side-effects to platinum-containing therapeutics. Tested in chick embryo cancer model and in-vitro cell lines

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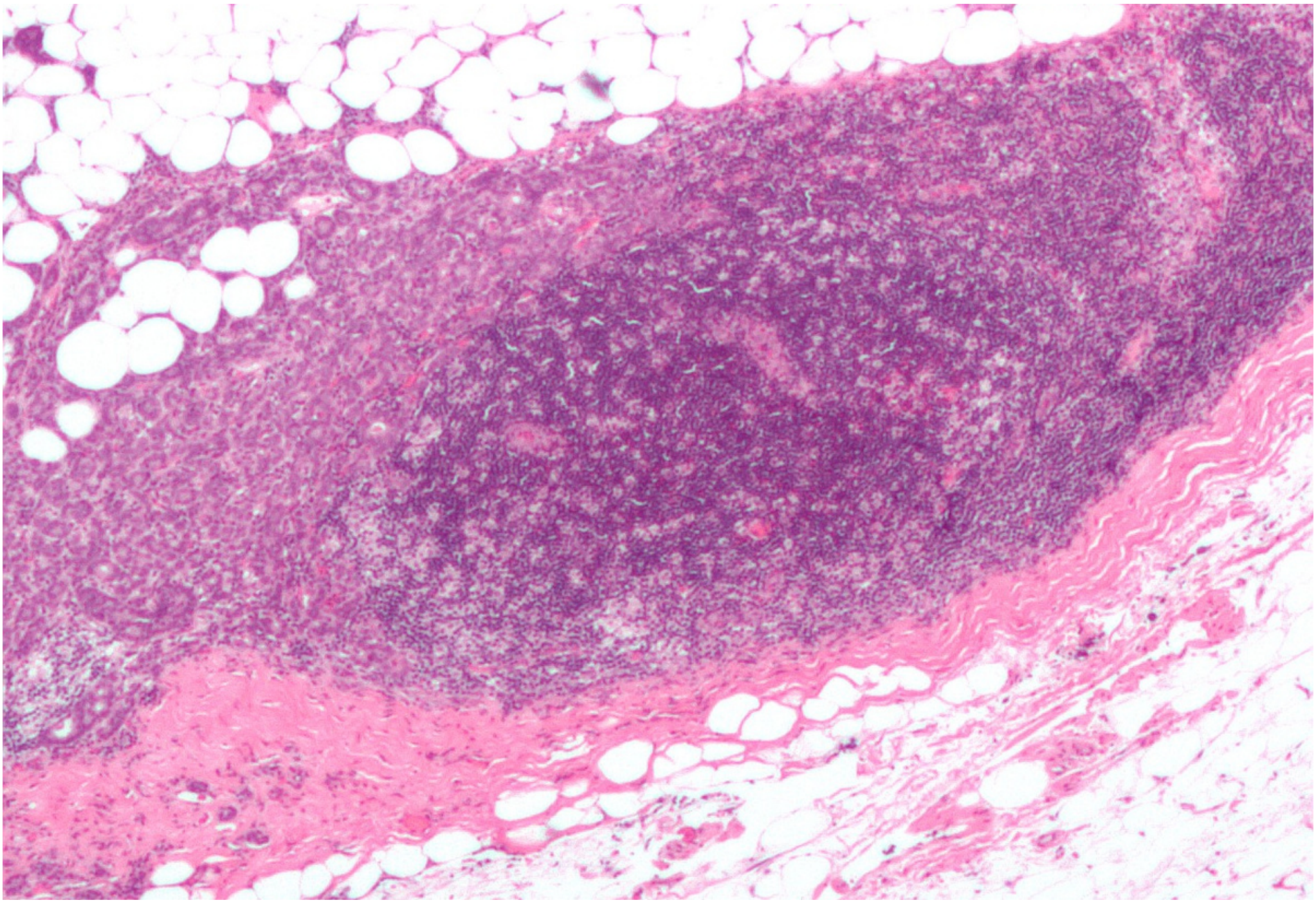

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Background

Palladium is less toxic than conventional platinum chemotherapies widely used to treat cancers and this may reduce the side-effects associated with conventional chemotherapies.

Platinum chemotherapeutics are used especially in patients with highly metastatic triple negative breast cancers (TNBC). The chemotherapy is non-selective and toxic causing negative side effects that have been well documented. TNBC also readily acquires a resistance to platinum-based therapies.

Researchers at Stellenbosch University and the University of Cape Town have developed and tested a palladium-based anti-cancer therapeutic as an alternative novel chemotherapeutic - *Palladacycle*.

Unviersity of Cape Town data shows that *Palladacycle* minimizes the chances of cancers developing resistance to the chemotherapy and being less toxic it is anticipated that side-effects associated with platinum-containing chemotherapeutics will be reduced.

Technology Overview

The invention is a bi-nuclear palladium-containing anti-cancer therapeutic referred to as the *Palladacycle*.

The *Palladacycle* is an organo-metallic heterocycle containing an atom of palladium in the ring. It has shown **excellent *in-vivo*** and *in-vitro* activity against oestrogen receptor-positive and -negative breast cancers cells in culture. It has also shown activity *in-vitro* against other cancer cell lines, including advanced melanomas and aggressive sarcomas.

A series of different molecules have been developed, an early lead showing promising anti-cancer activity was found to be unstable. The next round lead molecule 'BTC2' has improved water solubility and has performed as well as, if not better in *in vitro* tests compared to the earlier candidate.

Compared to the widely used platinum-based chemotherapeutic drug, which has an IC50 of approximately 10µM, BTC2 displayed an IC50 of approximately 0.2µM in breast cancer and a range of sarcoma cell lines tested. The results suggest that, at a concentration of 50-fold less BTC2 is as effective at killing cancer cells, but with will likely display lower side-effects due to the reduced dose.

The current stage of development is at **Technology Readiness Level 3**.

The next phase of development will involve animal trials to investigate pharmacokinetic and pharmacodynamic activities.

Benefits

Pre-clinical *in-vitro* and *in-vivo* trials in two common breast cancer cell lines, including the TNBC, have shown that the novel *Palladacycle* complex:

- is effective in arresting tumour growth at considerably lower concentrations than cisplatin,
- inhibits metastasis of breast cancer cells, and
- exhibits low toxicity effects.

Palladacycle has also been shown to be comparable to clinically approved anti-cancer agents, despite being tested at a dosing rate half that of Paclitaxel in a chick embryo model.

Palladacylce results against pxl

In addition to its confirmed minimal toxicity and commercially-comparable efficacy, the patent-pending *Palladacycle* can be synthesized chemically, so manufacture may be more cost-effective than other clinically approved anti-cancer agents. Furthermore, the lower dosage rate required due to the high potency of the drug as well as the lowered toxicity for equivalent efficacy is indicative of a reduced risk of associated side effects.

Applications

VALUE PROPOSITION & BENEFITS

The *Palladacycle* complex shows great potential as an alternative existing platinum-based chemotherapies:

- Palladium is less toxic than conventional platinum chemotherapies and may have a reduction in the side-effects associated with platinum-containing chemotherapies.
- Potential reduction in dose and exposure due to increased efficacy
- Lower-cost production by chemical synthesis

Opportunity

UCT is looking for Commercial partners to collaborate with and fund further development. The researchers and infrastructure at UCT will enable funded work to complete TRL 5. UCT also has considerable experience in running clinical trials for global pharmaceutical companies.

The current stage of development is at **Technology Readiness Level 3.**

The next stage activities includes animal model work and to conduct pharmacokinetic and pharmacodynamic activities.

Patents

- International Patent Application PCT/IB2019/051223
- International Patent Application PCT/IB2018/050957
- South African national phase patent application number 2018/01074 (Granted)
- South African national phase patent application number 2019/00976 (pending)
- European (EP) regional phase patent application number 19708680.4 (pending)
- United States (USA) national phase patent application number 16/960,967 (pending)

IP Status

- Patent application submitted

Seeking

- Development partner
- Licensing
- Seeking investment

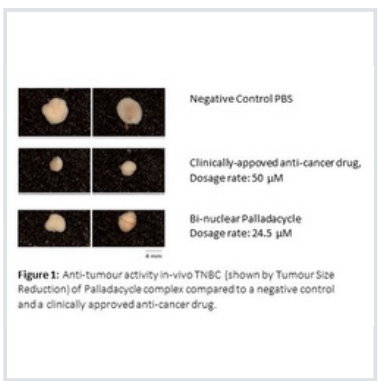

Figure 1: Anti-tumour activity in-vivo TNBC (shown by Tumour Size Reduction) of Palladacycle complex compared to a negative control and a clinically approved anti-cancer drug.