QBiotics Group Limited
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# Using veterinary to human parallel development to speed drugs to market

**Following its success in the veterinary market, QBiotics is now developing tigilanol tiglate for use against solid tumors in humans via intratumoral injection.**

QBiotics, a public unlisted Australian company, is combining its scientific expertize with experience and validation gained from its successful launch on the veterinary market to develop tigilanol tiglate, a small molecule used to treat solid tumors, for use in humans through direct intratumoral injection.

## The science behind tigilanol tiglate

A single intratumoral injection of tigilanol tiglate rapidly and completely destroys the injected tumor through local inflammation, by disrupting the blood vessels supplying the tumor, and through a process of cell death known as oncosis. Non-injected tumors may also be resolved, mediated by systemic anti-tumor immune responses (Fig. 1).

QBiotics has observed strong efficacy signals in a phase 1 trial of 22 patients with a broad range of cutaneous and subcutaneous solid tumors, with tigilanol tiglate treatment being generally well tolerated (ACTRN12614000685617). One-fifth of the patients experienced a complete response, with total tumor destruction, 28% achieved a partial response, and 12% of patients had stable disease. Although phase 1 trials are not powered for efficacy, the collective responses observed in this study equate to an overall injected-tumor response rate of 60% from a single injection. Non-injected tumor responses in distal tumors were also reported in two patients with metastatic melanoma.

In humans, tigilanol tiglate has potential as both a monotherapy and a combination therapy, and QBiotics is exploring both avenues in clinical trials. In a phase 1b/2a monotherapy trial, patients with unresectable head and neck squamous cell carcinoma (HNSCC) are given a single injection of tigilanol tiglate to evaluate tumor destruction (ACTRN12619001407189). In a phase 1b/2a study carried out in collaboration with MSD (trade name of Merck & Co. Inc., Kenilworth, USA), patients with checkpoint-inhibitor-refractory unresectable melanoma are given up to three doses of tigilanol tiglate in combination with MSD's immunotherapeutic Keytruda (pembrolizumab) (NCT04834973). Further phase 2a trials in patients with unresectable melanoma, HNSCC or soft-tissue sarcoma are in late-stage planning.

## Building a future through partnerships

In contrast with radiation and systemic therapies, intratumoral injections target tumor cells directly, limiting exposure to healthy tissue. Historically, intratumoral drugs have been disappointing; they can require multiple doses and often have only a local effect. Because tigilanol tiglate can completely destroy a tumor with a single treatment, and potentially shrink non-injected tumors, it has the potential for improved efficacy over other intratumoral treatments. It may significantly improve outcomes for patients with unresectable tumors, tumors in locations that are difficult to access, or where surgery could affect patients' ability to hear, see, smell, swallow or taste.

"We have seen evidence that tigilanol tiglate alone has potential against a range of tumors and has additive anti-tumor responses when combined with other cancer therapeutics, including chemotherapy, radiotherapy and checkpoint inhibitors," said Victoria Gordon, managing director and CEO of QBiotics.

The company is now seeking co-development and/or licensing partners among pharmaceutical companies to assist in the acceleration and expansion of tigilanol tiglate for multiple oncology indications.

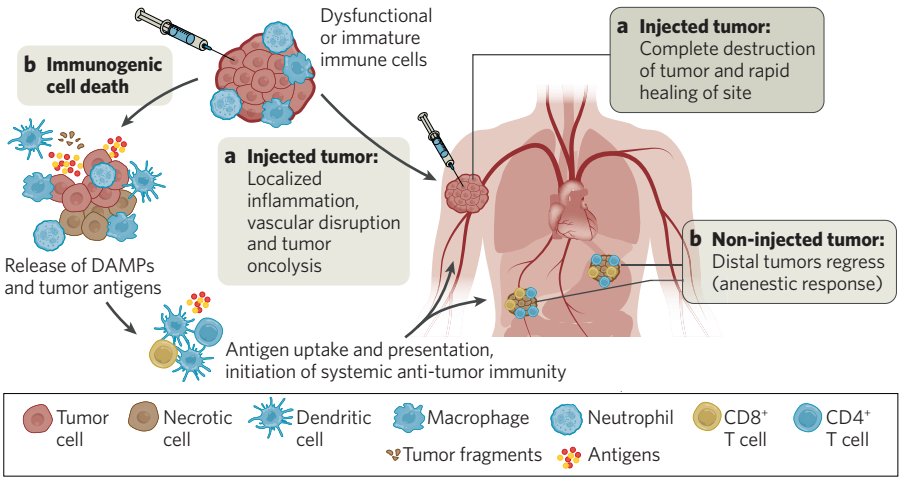


**Fig. 1 | Intratumoral treatment with tigilanol tiglate induces injected and systemic non-injected tumor responses. (a)** Injected tumors are rapidly destroyed by tumor cell necrosis and vascular disruption. **(b)** Non-injected neighboring or distant tumors regress by immune-mediated mechanisms. DAMPs, damage-associated molecular patterns.

## Validating the data

QBiotics' research has been validated through non-clinical and clinical studies carried out with an international network of academic and commercial partners.

In dogs, tigilanol tiglate provides a first-line alternative to surgery in non-metastatic mast-cell tumors, meeting an unmet need in the veterinary market. Its launch as Stelfonta in USA, Europe and Australia has provided QBiotics with an income stream, powering the company for future growth.

These spontaneous tumors in animals provide a clinically relevant and highly validated model for cancer in humans. Efficacy and safety studies carried out in dogs as part of the canine registration for Stelfonta will also form part of the non-clinical data package for regulatory authorities for approval in humans.

"Targeting the same therapeutic area in animals and humans means that we can develop quicker-to-market veterinary products at a relatively low cost, while forming the non-clinical evidence required for treating cancer in humans. It helps de-risk human clinical development and allows us to resolve many of the questions relating to efficacy, safety and manufacturing," said Gordon.

In a pivotal multicentre study in 123 canine patients with mast-cell tumors, a single injection induced a 75% complete response, and two injections led to an 88% complete response. One year later, 89% of the dogs had no tumor recurrence.

"These results gave us confidence to move into human clinical development and allowed us to pursue a global development plan along with a strong foundation for investment support," said Gordon.

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