Australian Government
Department of Health
Office of the Gene Technology Regulator

27 September 2021

Summary of Licence Application DIR 187

VRT Pharmaceuticals Pty Ltd has made an application under the *Gene Technology Act 2000* (the Act) to conduct a clinical trial using a genetically modified organism (GMO).

Project Title	Clinical trial of a genetically modified alphavirus for treatment of cancer
Parent organism	*Getah virus* (M1 strain), a member of the *alphavirus* genus
Genetic modifications	Two single nucleotide changes have been introduced into the *Getah virus* (M1) genome, each altering one amino acid in separate viral proteins.
Principal purpose	The trial will evaluate the safety and tolerability of the GMO in adult participants with locally advanced or metastatic cancer. Trial participants' immune response to the GMO, as well as its biodistribution and shedding, will also be assessed.
Previous clinical trials	The proposed study is the first formal clinical trial to be undertaken. However, nine patients with different solid tumours have been treated with the GMO under compassionate use access in China. A further five patients with advanced/metastatic liver cancer are currently receiving treatment.
Proposed limits and controls	
Proposed duration	5 years
Proposed number of participants	Up to twelve participants will be enrolled in the trial
Proposed location	Flinders Private Hospital, Bedford Park SA
Proposed controls	• The GMO will be administered to trial participants in a hospital setting • Staff preparing and administering the GMO will use personal protective equipment • Waste that may contain the GMO will be disposed of via the clinical waste stream • Participants will remain in hospital for at least 24 hours after the first treatment and 2 hours after subsequent treatments • Trial participants will take the following precautions: – avoid exposure to mosquitoes for 7 days after each treatment – if sexually active, use barrier contraception for 30 days after treatment – avoid contact with newborns, immunocompromised and severely immunodeficient individuals • Pregnant women will be excluded from the trial • Trial participants may not donate blood or organs during the trial • Immunocompromised or pregnant staff should avoid direct contact with the GMO and with participant injection sites, excreta and secretions

The application

Oncolytic viral therapy is a relatively new approach to cancer treatment. Oncolytic viruses (OVs) are intended both to selectively destroy cancer cells and activate the immune system, which is often suppressed within tumours. Globally, three OVs have been approved for therapeutic use and over thirty others are under clinical development.

The proposed clinical trial will evaluate the safety and tolerability of a genetically modified (GM) OV in adults with cancer that is locally advanced or has spread throughout the body. The GMO was modified from the M1 strain of *Getah virus*, which has been shown to preferentially target cancer cells and itself is under investigation as an OV. The genetic modifications enhance this selectivity, increasing viral replication in cancer cells but not in normal cells. In patients treated with the GMO under compassionate use access, reported adverse events were mild, self-limiting, and consistent with those seen with other OVs.

The applicant proposes to administer the GMO to trial participants in a hospital setting. Twelve participants would receive up to seven treatment cycles in which one of four increasing doses of the GMO is delivered intravenously. Patients who respond well to the treatment would have the opportunity to continue for another two years after the study protocol is complete. Participants would preferentially be recruited from the local area, but could live elsewhere in Australia and return to their homes in between treatments.

The application is for limited and controlled release under section 50A of the Act, as the Regulator is satisfied that its principal purpose is to enable the applicant to conduct a clinical trial, and the proposed limits and controls are such that consultation with prescribed experts, agencies and jurisdictions is not required at this stage. The proposed clinical trial must meet Therapeutic Goods Administration (TGA) requirements and would need approval from a registered Human Research Ethics Committee before commencing.

Next steps

The Gene Technology legislation sets out what the Regulator must do, as well as what the Regulator can or must consider, before deciding whether or not to issue a licence for this application.

The Regulator's staff will prepare a consultation version of the Risk Assessment and Risk Management Plan (RARMP) considering aspects of the application including the proposed limits and controls in accordance with the legislation.

The Regulator will seek comment on the consultation RARMP from the public, as well as a wide range of experts, agencies and authorities. The public and experts will be invited to provide submissions on the risks to human health and safety, and on risks to the environment from the proposed release.

At this stage, the consultation RARMP is expected to be released for comment in late November 2021.

After consultation, the Regulator's staff will finalise the RARMP, taking into account advice on relevant matters. The finalised RARMP will form the basis of the Regulator's decision whether or not to issue a licence. The consultation and final versions of the RARMP and associated documents will be available on the OGTR website when they are released.

Other information available from the OGTR website:

- information on Australia's national scheme for regulation of gene technology and
- information on the DIR application process.

Please use the contact details below, if you

- would like a copy of the application. Please include the identifier DIR 187.
- have any questions about the application or the legislated evaluation process or
- wish to register on the mailing list.

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