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Our Reference
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CONFIDENTIAL

To whom this may concern

I have been asked by Thomas Zetterberg, CEO of Canqura, Härkebergaby 6, 745 96 Enköping in Sweden ("Canqura") to provide an assessment of certain patents and patent applications ("Canqura patent portfolio") owned by Canqura. For the sake of good order, I note that I currently represent Canqura on the prosecution of parts of the Canqura patent portfolio.

Background

The Canqura patent portfolio consists of the **"Killcan" family** which derives from the PCT application WO 2008/063129 filed in 2007, and the **"G3" EP application** which derives from WO 2013/051994 filed in 2012. Both application families relate to the use of certain (nano)particles in cancer therapy.

The inventions described in the two application families mainly differ in the way the (nano)particles have been defined (*i.e.* what they contain and their morphology).

The "Killcan" family members (EP, US, CA, AU, CN and JP) have all been granted. Due to national differences in patent office prosecution, the granted national patents have slightly different protective scope.

The "G3" EP application has not yet been granted, but an "Intention to Grant" has been received from the EPO in June 2022. The claims allowed for grant are therefore already known, and it is expected that the final grant will be announced in Q1 2023.

Protection scope

The main claim (claim 1) of each patent document will in the following be briefly commented on.

"Killcan" family

The main claim of the **international PCT application** (WO 2008/063129) read:

1. **Use of lipid containing particles comprising at least one lipid and at least one saponin for the preparation of a pharmaceutical for the treatment of cancer.**

During national prosecution the above claim was limited according to local/national practice.

In **Europe** the patent (EP2094278 B1) was granted with the following main claim:

1. **Use of iscom matrix particles comprising at least one lipid chosen from cholesterol and phospholipid and at least one saponin, wherein the saponin is a crude saponin fraction from *Quillaja Saponaria* Molina or a sub fraction thereof which particles do not contain cancer antigens, for the preparation of a pharmaceutical for the treatment of cancer.**

The regional European (EP) patent has been validated in a number of European countries. As of June 2022, the EP patent is in force in **IT, DE, ES, SE, DK, GB** and **FR**.

In **USA**, the patent (US9040081 BB) was granted with the following main claim:

1. **A method for the treatment of cancer wherein an iscom matrix particle comprising at least one lipid selected from cholesterol and phospholipid and at least one saponin, chosen from fraction A and fraction C from *Quillaja saponaria* Molina or a sub fraction thereof, which particle does not contain cancer antigens, is administered to an individual in need of cancer treatment.**

In **Canada**, the patent (CA2669209 C) was granted with the following main claim:

1. **Use of lipid containing iscom matrix particles comprising at least one lipid and at least one saponin, which particles do not contain cancer antigens for the preparation of a pharmaceutical for the treatment of cancer.**

In **Australia**, the patent (AU2007322424 BB) was granted with the following main claim:

1. **Use of a pharmaceutical consisting essentially of lipid containing particles comprising at least one lipid and at least one saponin in the preparation of a medicament for the treatment of cancer, wherein said particles do not contain cancer antigens.**

In **China**, the patent (CN101563090 B) was granted with the following main claim:
(Machine translation, to be verified)

1. **Use of an immunostimulatory complex [iscom] matrix lipid-containing particle consisting of at least one lipid and saponins from Fraction C of *Quillaja Saponaria* Molina or a subfraction thereof for the preparation of a medicament for the treatment of cancer.**

In **Japan**, the patent (JP5301455 B2) was granted with the following main claim:
(Machine translation, to be verified)

1. **Lipids containing particles with at least one lipid and at least one crude saponin fraction from *Quillaja Saponaria* Molina or its subfractions for producing pharmaceuticals for the treatment of cancer, without cancer antigens.**

The "Killcan" patents in **Europe, US, Canada** and **China** cover the use of ISCOM matrix particles in cancer treatment. ISCOM matrix particles are defined in the patent description as *40 nm spheres built up by 6nm ring formed sub-fragments* and contain at least one lipid and at least one saponin and does not contain a cancer antigen. ISCOM matrix particles usually also comprise a phospholipid, although this is not mandatory.

The "Killcan" patents in **Australia** and **Japan** are not limited to ISCOM particles, so these patents more broadly cover the use in cancer treatment of particles of any shape or composition, as long as the particles contain at least one lipid and at least one saponin and does not contain a cancer antigen.

The Killcan patent family will expire in November 2027, possibly with extensions in some countries (to be verified).

"G3" EP application[1]

The other part of the Canqura patent portfolio is the G3 EP patent, which is derived from the international PCT application **WO 2013/051994**.

The main claim of WO 2013/051994 reads:

1. **Nanoparticles comprising sterol, preferably cholesterol and a component from *Quillaja saponaria* Molina selected from quillaja acid and quillaja saponin, characterized in that said nanoparticles do not comprise a phospholipid.**

WO 2013/051994 was continued nationally in Europe, resulting in the granted product patent **EP2750683** now owned by Croda International, which relates to the G3 particles as such. The main claim reads:

1. **Stable nanoparticles comprising sterol, preferably cholesterol and a component from Quillaja Saponaria Molina which is quillaja saponin fraction QHA, QHB and/or QHC, characterized in that said nanoparticles do not comprise a phospholipid, have a particle diameter in the range of 15-25 nanometers and wherein the ratio between cholesterol and quillaja saponin is from 1:2 to 2:1.**

[1] The nanoparticles claimed in WO 2013/051994 are referred to by the inventors as "G3" particles.

Before grant of EP2750683 the cancer treatment divisional application **EP3311827** was filed. The allowed main claim[2] of EP3311827 reads:

1. **Nanoparticles comprising sterol, preferably cholesterol and at least one component from *Quillaja saponaria* Molina selected from quillaja acid and quillaja saponin, for use in the treatment in a human of cancer, characterized in that said nanoparticles do not comprise a phospholipid.**

The allowed claim of EP3311827 broadly covers the use in cancer treatment of nanoparticles of any shape or composition, as long as the particle contain sterol (e.g. cholesterol) and at least one quillaja saponin and does not contain a phospholipid. The particles covered by the product patent EP2750683 are thus in comparison more narrowly defined than in the cancer treatment patent EP3311827. This is due to limitations incurred in the European prosecution phase and later in opposition of the product patent application.

The G3 cancer treatment EP patent will expire in 2032, i.e. about 5 years after the Killcan patents.

Yours sincerely,

AWA Denmark A/S

Michael Bech Sommer

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[2] An Intention to Grant communication from the EPO has been received in June-22. It is intended to request a delay in grant, such that Canqura can obtain a Unitary Patent in Q1-Q2 2023 when this option becomes available.