No. S-169829
Vancouver Registry

In the Supreme Court of British Columbia

Between

Acuitas Therapeutics Inc.

Plaintiff

and

Arbutus Biopharma Corporation

Defendant

RESPONSE TO CIVIL CLAIM

Filed by: Arbutus Biopharma Corporation ("**Arbutus**")

PART 1: RESPONSE TO NOTICE OF CIVIL CLAIM FACTS

Division 1 – Response to Facts

1. Except where expressly admitted, Arbutus denies each and every allegation of fact in the Notice of Civil Claim and puts the Plaintiff, Acuitas Therapeutics Inc. ("**Acuitas**"), to the strict proof thereof.

2. The facts alleged in paragraphs 1, 2, 3, 5, 6 (as to the fact that Arbutus sent a letter to Acuitas on 29 August 2016 advising it of material breaches of Acuitas' obligations and terminating the Cross License Agreement), 10 and 11 of Part 1 of the Notice of Civil Claim are admitted.

3. The facts alleged in paragraphs 4, 7, 8, 9, and 14 of Part 1 of the Notice of Civil Claim are denied.

4. The facts alleged in paragraphs 12 and 13 of Part 1 of the Notice of Civil Claim are outside the knowledge of Arbutus.

5. Capitalized terms used in this Response have the meanings ascribed to them in the Notice of Civil Claim, unless specified otherwise.

Division 2 – Defendant's Version of Facts

A. The Parties

6. Arbutus is a publicly-traded biopharmaceutical company with pioneering expertise in developing lipid nanoparticle ("**LNP**") technology, which is used to deliver nucleic acids into human cells to treat disease.

7. Acuitas is a private company founded in 2009. It is also involved in developing LNP technology.

B. The Technology

8. Arbutus' LNP technology is used to encapsulate one or more strings of specific sequences of nucleic acid (also referred to as the "payload"). The LNP allows the nucleic acid to be transported safely through the bloodstream and released inside the desired cells with minimal side effects. Thus, LNP has two basic components: the lipid carrier component and the nucleic acid payload.

9. Each lipid carrier is composed of three to four different types of lipids. In order to control where within the body the lipid nanoparticle releases its nucleic acid payload, and other critical factors such as the timing and efficacy of the release, Arbutus developed multiple proprietary lipids, formulation schemes and manufacturing processes. By varying the specific lipids employed in its particles and changing the ratios of the different lipids to each other, as well as to the nucleic acid payload they encapsulate, Arbutus is able to fine-tune its technology to maximize therapeutic performance.

10. Among the many uses of Arbutus' LNP technology is in gene therapy applications. Gene therapy describes the transfer of RNA[1] (specifically, messenger RNA or "mRNA") or DNA into human cells to achieve the deletion, insertion or replacement of regions of interest in specific disease-causing genes.

11. The specific gene that a given LNP formulation is meant to act on is referred to as the "target". The nucleic acid sequences included in the payload correspond to only a small portion of the target gene. Accordingly, another important feature of product performance involves selection of the exact nucleic acid sequences, or set of sequences, to include in the payload.

12. Each pharmaceutical "product" utilizing LNP is comprised of a specific nucleic acid sequence, or set of sequences, encapsulated within the LNP as the payload, as well as the specific LNP formulation itself. As a result, there can be a number of unique products directed to the same target that vary with respect to which nucleic acid sequences are utilized and/or the specific formulation that is used (both with respect to the lipids that are utilized and the specific ratios used for those lipids).

13. Regulatory agencies require separate regulatory filings and clinical support for each unique product (*i.e.* each combination of a specific carrier formulation with a specific nucleic acid sequence), regardless of whether they act on the same target and/or encapsulate the same payload.

C. The Cross-License Agreement

14. On 12 November 2012, pursuant to the provisions of a settlement agreement, Acuitas, Tekmira (Arbutus' predecessor) and Protiva Biotherapeutics Inc. ("**Protiva**" - a wholly owned subsidiary of Tekmira) entered into a cross-license agreement in which Acuitas received a limited license to certain LNP patents held by Tekmira. In exchange, Tekmira was granted a license to certain of Acuitas' technology (the "**Cross-License Agreement**").

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[1] RNA (ribonucleic acid) is a critical component of protein synthesis in the human body, and acts as a messenger between DNA and ribosomes, which ultimately produce the protein.

15. Section 2.1 of the Cross-License Agreement sets out the limited license granted to Acuitas:

> Subject to the terms and conditions of this Agreement, TPC and Protiva (each to the extent they Control the Tekmira Combined Licensed Technology and the Category 1 Patents) hereby grant to Acuitas, under the Tekmira Combined Licensed Technology and Category 1 Patents, a worldwide, non-exclusive right and license to Research, Develop and Commercialize Supplemental Field Products...which right and license may be sublicensed by Acuitas in accordance with the provisions of Section 2.2. [Emphasis added]

16. Supplemental Field Products are defined in the Cross-License Agreement as follows:

> "Supplemental Field Product" means a product containing, comprised of, or based on Antisense or Gene Therapy.
>
> "Supplemental Field" means the delivery of: (i) single-stranded oligonucleotides, either chemically modified or unmodified, acting through the RNase H mechanism or by or other mechanisms of translational arrest but excluding RNA interference involving RISC ("**Antisense**") and (ii) DNA plasmids or messenger RNA ("**mRNA**") either chemically modified or unmodified that are transcribed and/or translated into protein and wherein the pharmacological activity is dependent on expression of the protein ("**Gene Therapy**").

17. Section 2.2 of the Cross-License Agreement limits the scope of Acuitas' sublicensing rights. Pursuant to that section, Acuitas may only grant sublicenses "on a Sublicensable Product-by-Sublicensable Product basis".

18. "Sublicensable Product" is defined as:

> A Supplemental Field Product that has been developed by Acuitas and for which Acuitas has shown (i) in the case of an Antisense product, a pharmacological effect of that product against the Target or (ii) in the case of a Gene Therapy product a pharmacological effect resulting from expression of the protein, in both cases in *in vivo* studies in a small animal species.

19. Accordingly, under Sections 2.1 and 2.2 of the Cross License Agreement, Acuitas has a limited right to sublicense to third parties a subset of Supplemental Field Products: those which Acuitas has already developed using Arbutus' technology, and for which Acuitas has already demonstrated a pharmacological effect in small animal studies.

20. The Cross-License Agreement does not grant Acuitas any right to sublicense other technology or rights to third parties (*e.g.* the right to use Arbutus' technology to develop a drug for a particular disease or other target), nor does it permit third parties to use, develop, manufacture or gain any other rights in or to Supplemental Field Products until after Acuitas has demonstrated that the particular product is a "Sublicensable Product".

21. In summary:

(a) Acuitas has limited sublicensing rights under the Cross-License Agreement. Among other requirements, Acuitas may not grant any sublicense under the Cross-License Agreement unless the sublicense is for a specific formulated product (*i.e.* is a product license) that:

(i) contains, comprises or is based on Antisense or Gene Therapy, as defined by the Cross-License Agreement;

(ii) has been developed by Acuitas; and

(iii) for which Acuitas has shown a pharmacological effect in an *in vivo* small animal study;

(the "**Sublicensing Obligations**") and

(b) Acuitas' own license from Arbutus is also restricted. Acuitas is only permitted to use Arbutus' technology to "Research, Develop and Commercialize Supplemental Field Products". Acuitas is not permitted to sell or provide Arbutus' technology to third-parties except as a Supplemental Field Product (the "**Access Obligations**").

22. Section 9.1(b) of the Cross-License Agreement states:

> (b) This agreement may be terminated by either Party:
>
> (i) upon any material breach by the other Party of any material obligation of such Party under this Agreement, such termination to be effective thirty (30) days, in the case of non-payment of any amount due, and sixty (60) days (each

> such period a "**Cure Period**"), in the case of any other material breach, after receipt by the breaching Party of written notice of termination from the non-breaching Party describing such material breach of this Agreement in reasonable detail...

23. The terms of the Cross-License Agreement are known to Acuitas, and will be relied upon at the trial of this action for their full and precise meaning and effect.

C. Acuitas' Sublicense to Moderna

24. In or around May 2015, Acuitas granted a sublicense to Moderna Therapeutics ("**Moderna**"), purportedly under the Cross-License Agreement (the "**Moderna Sublicense**"). The Moderna Sublicense purported to grant Moderna a sublicense to "any and all Know-How, Patents and Materials" that covered LNP technology, was licensed to Acuitas, and that "may be necessary or useful to Develop or Commercialize" products directed at a specific target.

25. In or around June 2016, Arbutus became aware that Acuitas had breached the Cross-License Agreement by, among other things, entering into the Moderna Sublicense and the "Development and Option Agreement" that preceded the Moderna Sublicense. Specifically, and without limitation, Arbutus became aware that:

(a) Moderna (and possibly others) were assisting or otherwise collaborating with Acuitas, using Arbutus' technology without a license;

(b) Acuitas had purported to grant a sublicense to Moderna before it had developed any Sublicensable Product;

(c) the Moderna Sublicense purported to grant Moderna a "target license" (*i.e.* a broad right to use Arbutus' technology to develop products aimed at a specific target) rather than a "product license" (*i.e.*, a specific formulated product);

(d) the Moderna Sublicense was to a vaccine, which is neither antisense technology, nor gene therapy; and

(e) the purported sublicense to Moderna otherwise did not comply with the definition of a Supplemental Field Product.

26. In or around July 2016, Arbutus wrote to Acuitas identifying the foregoing breaches, requesting further information regarding the Moderna Sublicense, and demanding that Acuitas take steps to comply with the Cross-License Agreement.

27. Acuitas did not deny that it was using its license to develop products jointly with third parties and it confirmed that it had granted a sublicensing option to Moderna before the sublicensed product had been tested in a small animal species, but refused to take any corrective action.

28. On or around 26 August 2016, Arbutus became aware that Acuitas had entered into a second sublicense with Moderna which is substantially the same as the Moderna Sublicense, but is directed to a different target (the "**Second Moderna Sublicense**"). For the same reasons set out in paragraph 25, the Second Moderna Sublicense breaches the Cross-License Agreement.

29. Acuitas has further breached its Access Obligations and its Sublicensing Obligations by providing Arbutus' technology to other third parties, the particulars of which are within the knowledge of Acuitas.

D. Termination of the Cross-License Agreement

30. On 29 August 2016, Arbutus advised Acuitas that it was exercising its right to terminate the Cross-License Agreement pursuant to Section 9.1(b) due to, among other things, Acuitas' breaches of its Sublicensing Obligations and its Access Obligations.

31. On 21 October 2016, Acuitas asserted that Arbutus' allegations were "non-existent" and that as a result, it considered Arbutus' notice of termination to have been "deemed automatically withdrawn and . . . of no further legal force or effect".

32. On 24 October 2016, Arbutus reiterated Acuitas' breaches of the Cross-License Agreement and confirmed its termination of the Cross-License Agreement.

33. The 60-day cure period contemplated by Section 9.1(b) the Cross-License Agreement ended on 31 October 2016.

34. Acuitas failed or refused to cure its breaches, and the Cross-License Agreement terminated as of the end of the day on 31 October 2016.

Division 3 – Additional Facts

35. See above

PART 2: RESPONSE TO RELIEF SOUGHT

36. Arbutus consents to the granting of the relief sought in the following paragraphs of Part 2 of the Notice of Civil Claim: ***None***.

37. Arbutus opposes the granting of the relief sought in the following paragraphs of Part 2 of the Notice of Civil Claim: ***All***.

38. Arbutus takes no position on the granting of the relief sought in the following paragraphs of Part 2 of the Notice of Civil Claim: ***None***.

PART 3: LEGAL BASIS

A. Acuitas Materially Breached the Cross-License Agreement

39. Acuitas materially breached the Cross-License Agreement by, without limitation, breaching its Sublicensing Obligations and its Access Obligations as follows:

(a) granting sublicenses for the use of Arbutus' technology towards a certain target (as opposed to the narrower product licenses permitted under the Cross-License Agreement);

(b) further and in the alternative, granting sublicenses for products that are not Supplemental Field Products (*i.e.*, are not an Antisense or a Gene Therapy product);

(c) further and in the alternative, granting sublicenses and/or sublicensing options for Supplemental Field Products prior to demonstrating their pharmacological effect in a small animal study;

(d) further and in the alternative, granting sublicenses for products that were not developed by Acuitas;

(e) further and in the alternative, providing and/or selling Arbutus' technology to third parties independent of a Supplemental Field Product; and

(f) further and in the alternative, encouraging or permitting third parties to use Arbutus' technology without a license or sublicense

B. Arbutus is Entitled to Terminate the Cross-License Agreement

40. Pursuant to Section 9.1(b) of the Cross-License Agreement, Arbutus is entitled to terminate the Cross-License Agreement if Acuitas commits a material breach of a material obligation under Cross-License Agreement, and such breach remains uncured after 60 days.

41. The Sublicensing Obligations and the Access Obligations are material obligations under the Cross-License Agreement.

42. Acuitas' wrongful conduct constitutes material breaches of the Sublicensing Obligations and the Access Obligations.

43. Acuitas failed or refused to cure its breaches, and the Cross-License Agreement terminated as of the end of the day on 31 October 2016.

44. Further and alternatively, to the extent the Court concludes that the cure period contemplated by the Cross-License Agreement is tolled during the pendency of this proceeding, the Cross-License Agreement terminates on the date of final judgment in this proceeding.

45. In response to paragraphs 9 and 10 of Part 1, and paragraphs 3 and 4 of Part 3 of the Notice of Civil Claim, Arbutus specifically denies that its termination of the Cross-License Agreement constituted anticipatory or wrongful repudiation. Arbutus terminated the Cross-License Agreement in accordance with its terms.

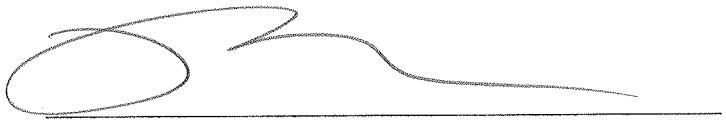
D. Acuitas Has Suffered No Damages

46. In response to paragraph 14 of Part 1, and paragraph 5 of Part 3 of the Notice of Civil Claim, Arbutus specifically denies that Acuitas has suffered the alleged or any loss or damage, and puts Acuitas to the strict proof thereof.

47. Further and in the alternative, if Acuitas has suffered any loss or damage as alleged or at all (which is not admitted and is expressly denied), the loss or damage was not a result of any act or omission for which Arbutus is at law responsible as alleged or at all.

Arbutus Biopharma Corporation's address for service:	BORDEN LADNER GERVAIS LLP 1200 Waterfront Centre 200 Burrard Street P.O. Box 48600 Vancouver, British Columbia V7X 1T2 Attention: Robert J.C. Deane
Fax number address for service (if any):	None
E-mail address for service (if any):	None

Date: 15 November 2016



Signature of

☐ defendant ☑ lawyer for the defendant, Arbutus Biopharma Corporation,
Robert J.C. Deane

Rule 7-1 (1) of the *Supreme Court Civil Rules* states:

(1) Unless all parties of record consent or the court otherwise orders, each party of record to an action must, within 35 days after the end of the pleading period,

(a) prepare a list of documents in Form 22 that lists

(i) all documents that are or have been in the party's possession or control and that could, if available, be used by any party at trial to prove or disprove a material fact, and

(ii) all other documents to which the party intends to refer at trial, and

(b) serve the list on all parties of record.

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RESPONSE TO CIVIL CLAIM

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