IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ACUITAS THERAPEUTICS INC.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C.A. No. 22-_____
	)	
GENEVANT SCIENCES GMBH, AND ARBUTUS BIOPHARMA CORP.	)	
	)	
Defendants.	)	
	)	

COMPLAINT FOR DECLARATORY JUDGMENT OF NON-INFRINGEMENT AND INVALIDITY

Acuitas Therapeutics Inc. ("Acuitas"), for its Complaint against Genevant Sciences GmbH ("Genevant") and Arbutus Biopharma Corp. ("Arbutus"), alleges as follows:

NATURE OF THE ACTION

1. COVID-19 has presented the worst public health crisis in a century. Two years later, however, the pandemic is receding. That is in large part due to the amazing success story of the mRNA vaccines against the virus that causes COVID-19. Those vaccines exist only because of decades of hard work and ingenuity by the Plaintiff, Acuitas, and others, to develop the technology that allowed the rapid development of a vaccine to combat the pandemic.

2. Traditional vaccines create immunity by injecting a patient with pieces of the virus, or an inactive form of that virus. The vaccines that Acuitas helped to develop utilize messenger RNA ("mRNA") technology, do not require injection of the virus, and were developed much more quickly than traditional vaccines. All living organisms, including both humans and viruses, make proteins, which are the workhorses that complete the tasks needed by that organism. In humans

the "blueprint" for these proteins is carried in genes (i.e., DNA), but that blueprint needs to be converted into an mRNA message that tells the body to make a particular protein.

3. mRNA vaccines work by introducing into a person the mRNA message that instructs the body to make a foreign protein that is itself a piece of a virus. When that viral protein is made, or "expressed," by the person's cells, that person's immune system then recognizes that the protein is foreign and develops an immune response to it. If that person is later infected with the virus itself, his or her immune system is primed to protect against or minimize the significance of the viral infection. Because the mRNA contained in the vaccine represents a protein that is only a piece of the virus, the entire virus is never introduced into the body and there is thus no risk of infection from the vaccine.

4. For all of its advantages, however, working with mRNA presents prodigious challenges. First, mRNA is exceptionally fragile and, when injected into the body, breaks down extremely quickly. Second, mRNA is too large a molecule to enter into human cells on its own. An mRNA vaccine therefore requires a delivery system that protects the mRNA after it is injected into the person and transports the mRNA into the person's cells.

5. In the decade before COVID-19 emerged, Acuitas worked to solve that delivery-system problem: it painstakingly engineered a microscopic sphere of fats called a Lipid Nanoparticle, or "LNP," that can envelop and protect the mRNA. These mRNA-LNPs protect the fragile mRNA, allow it to cross the membrane of a human cell, and then release the mRNA so that it can be used to create the proteins that will in turn generate an immune response. One of Acuitas's mRNA-LNPs is used, under license, in Pfizer and BioNTech's COVID-19 vaccine, COMIRNATY®, which has been a global success in protecting people from COVID-19. To date, over 320 million doses of COMIRNATY® have been administered in the United States.

6. The defendants here, Arbutus and Genevant, had nothing to do with that success. Neither has a COVID-19 vaccine, neither has created any component of such a vaccine, and neither has commercialized an LNP that can effectively wrap and protect any mRNA molecule. On the contrary, only after COMIRNATY® achieved worldwide commercial success did Arbutus and Genevant emerge to make the spurious claim that COMIRNATY® may infringe Arbutus's patents, and, on information and belief, to demand hundreds of millions, if not billions, of dollars in wholly unjustified payments. Arbutus and Genevant seek the benefits flowing from COMIRNATY® without having borne any of the burden of developing it. Their claim to rights in—and payment for—COMIRNATY® is baseless.

7. What is now Arbutus was originally founded as Inex Pharmaceuticals Inc. in the early 1990s, by leading LNP scientists Dr. Pieter Cullis, Dr. Thomas Madden, and Dr. Michael Hope, to develop therapeutics incorporating lipid-based nanomaterials. This research led to the development of anticancer therapeutics that provided greater potency in fighting tumors while reducing the side effects often seen with such drugs. Subsequently, Inex (later known as Tekmira Pharmaceuticals Corp.) developed lipid nanoparticles to deliver new classes of drugs based on a type of nucleic acid called small interfering RNA, or "siRNA," which are short pieces of RNA that interfere with the body's ability to make certain proteins that may cause disease. Some of this research led to the development of an siRNA therapeutic called ONPATTRO®.

8. By 2008 the company that is now Arbutus was no longer interested in supporting the work that Dr. Madden and Dr. Hope were pursuing, and terminated their employment. Together with Dr. Cullis, Drs. Madden and Hope founded Acuitas Therapeutics Inc. (originally called AlCana Technologies Inc.) to develop LNP technology, and, by 2012, Acuitas had decided to focus on the development of LNP technology for the delivery of mRNA. Conversely, Arbutus

chose to focus its business on the much less challenging problem of developing LNP carriers to encapsulate siRNA.

9. There were good scientific reasons for Arbutus to have bet on siRNA therapeutics rather than mRNA therapeutics. Despite the similarity in their names, siRNA and mRNA are fundamentally different in ways that may frustrate the design of LNPs to encapsulate mRNA. For starters, there is the size difference: mRNA molecules are much larger than siRNA molecules, with the mRNA in COMIRNATY® some 200 times longer than an average siRNA molecule. Then there is the rigidity difference: siRNA molecules are akin to short, sturdy rods, while the longer mRNA molecules can fold and wind into complex shapes. The technology needed to wrap an siRNA molecule in a lipid nanoparticle is thus vastly different (and simpler) than what is needed to wrap an mRNA molecule. Importantly, mRNA is also much less stable than siRNA, significantly complicating mRNA's formulation and encapsulation in LNP and the manufacture of mRNA vaccines.

10. While the hope for an mRNA therapeutic is over thirty years old, mRNA's inherent instability and its inability to enter cells presented major barriers to its clinical use. In addition, previously known ways to package and deliver mRNA were either ineffective or toxic.

11. Acuitas's scientists solved those problems. They identified appropriate formulation conditions to allow efficient encapsulation of mRNA into LNPs and, importantly, to protect the mRNA from degradation during the formulation process. They tested hundreds of different LNPs with mRNA in order to determine the characteristics for successful encapsulation. And Acuitas's scientists, in collaborations with its partners, evaluated different LNPs for use in a variety of different vaccines. This research has been published in leading scientific journals, including in *Nature*.

12. Acuitas's research has also focused on the design and synthesis of novel lipids that provide more efficient and safe delivery of mRNA. This research has resulted in the identification of hundreds of novel lipids with improved activity and safety. Acuitas has also patented its novel discoveries, which include the ionizable cationic lipid known as ALC-0315, which is used in the LNP in COMIRNATY®. Acuitas and its researchers have received global praise, recognition, and awards for their role in developing the LNP technology required for mRNA vaccines, including the critical LNP component of COMIRNATY®. These awards include the 2021 Global Impact Award by Life Sciences British Columbia, the Prince Mahidol Award, the VinFuture Grand Prize, the BIAL Award in Biomedicine, and the admission of Dr. Pieter Cullis to the Order of Canada.

13. When Arbutus saw the tremendous success of the mRNA vaccines for COVID-19, it realized that having chosen to pursue siRNA therapeutics instead of mRNA was a bad decision, both scientifically and financially. Upon information and belief, Arbutus and Genevant sent a demand letter to Pfizer threatening to assert nine patents against the sale and use of the COMIRNATY® vaccine. That demand, and the prospect of future claims against other Acuitas licensees seeking to use Acuitas's LNPs for other mRNA vaccines and therapeutics, threaten to cause serious harm to Acuitas's business.

14. Acuitas therefore brings this action pursuant to Federal Rule of Civil Procedure 57 and 28 U.S.C. § 2201 for a declaratory judgment that the following nine Arbutus patents are not infringed by the manufacture, use, offer for sale, sale, or importation into the United States of COMIRNATY® and are, in any event, invalid: U.S. Patent Nos. 8,058,069 (the "'069 patent"); 8,492,359 (the "'359 patent"); 8,822,668 (the "'668 patent"); 9,006,417 (the "'417 patent"); 9,364,435 (the "'435 patent"); 9,404,127 (the "'127 patent"); 9,504,651 (the "'651 patent");

9,518,272 (the "'272 patent"); and 11,141,378 (the "'378 patent") (collectively the "Arbutus Patents").

THE PARTIES

15. Plaintiff Acuitas is a leading biotechnology company that collaborates with partner companies and academic institutions to develop new therapies to address unmet clinical needs. It is a Canadian corporation organized and existing in British Columbia, Canada, with a principal place of business at 6190 Agronomy Road, Suite 405, Vancouver, British Columbia, V6T 1Z3, Canada.

16. Acuitas itself specializes in the development of mRNA-LNP formulations for use as therapeutics. Acuitas has partnered with non-parties BioNTech and Pfizer to supply and license the LNP used in COMIRNATY®, a COVID-19 vaccine being administered to protect people around the world. COMIRNATY® has received full approval for use by the United States Food and Drug Administration ("FDA").

17. On information and belief, Defendant Genevant Sciences GMBH, an indirect wholly owned subsidiary of Genevant Sciences Ltd. (itself a Bermuda holding company), is a limited liability company organized and existing under the laws of Switzerland with a principal place of business at Viaduktstrasse 8, 4051 Basel, Switzerland.

18. On information and belief, Defendant Arbutus Biopharma Corp. (variously known in the past as Tekmira, Protiva, and Inex, and referred to herein as "Arbutus") is a corporation organized and existing under the laws of Canada with corporate headquarters at 1066 W. Hastings Street Suite 1600, Vancouver, British Columbia, V6E 3X1, Canada and with research headquarters at 701 Veterans Circle, Warminster, Pennsylvania 18974.

19. On information and belief, non-party Roivant Sciences Ltd. owns approximately 84% of Genevant Sciences Ltd., and Arbutus owns the remaining approximately 16% of Genevant Sciences Ltd. On information and belief, Roivant has offices at 151 W. 42nd Street, 15th Floor, New York, New York 10036. On information and belief, Roivant has acted as an agent for Arbutus and Genevant with respect to acts giving rise to this Complaint.

20. Arbutus is the owner of all rights, title and interest to each of the Arbutus Patents. Upon information and belief, Genevant holds a license to each of the Arbutus Patents.

JURISDICTION AND VENUE

21. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), and 2201.

22. This Court has personal jurisdiction over Genevant and Arbutus because each of them purposely availed itself of this jurisdiction by sending demand letters into this District alleging potential patent infringement. Specifically, on November 23, 2020 and October 12, 2021, Genevant and Arbutus sent letters to Pfizer's headquarters on 42nd Street in Manhattan, within this District, pursuant to 35 U.S.C. § 287(a), asserting that the making, use, sale, or offer for sale of COMIRNATY® may infringe each of the Arbutus Patents. On information and belief, Arbutus was aware of, and authorized and participated in, Genevant's sending of those letters, as Arbutus is a significant shareholder in Genevant and is the assignee of the patents that Genevant threatened to assert, and Arbutus's President and CEO signed both letters. By sending the letters, each of Genevant and Arbutus acted at least in part through their agent Roivant, which is itself headquartered in this District.

23. On information and belief, Pfizer and BioNTech sell COMIRNATY® in this District.

24. Arbutus's and Genevant's accusations that the making, use, sale, or offer for sale of COMIRNATY® may infringe each of the Arbutus Patents has caused Acuitas harm in this District, at least because it has impaired or affected Acuitas's ability to license its LNPs to companies headquartered or incorporated within this State and District, including Pfizer.

25. Venue is proper in this district pursuant to 28 U.S.C. §§ 1391(b) and (c), and 1400(b).

BACKGROUND

Acuitas

26. The founders of Acuitas, Drs. Madden, Cullis, and Hope, have been working on lipids and LNP formulations for drug delivery for decades, including at Acuitas and when they were at Arbutus's predecessor companies, Inex and Tekmira.

27. Acuitas designs and synthesizes novel lipids, such as cationic lipids and pegylated lipids, formulates those lipids with mRNA into LNPs, optimizes such formulations using scalable components and processes, and performs analytical and biophysical characterization and preclinical characterization of the LNPs to ensure they have the most advantageous safety and efficacy profiles.

28. Acuitas has synthesized hundreds of novel cationic lipids and has evaluated these novel compounds in mRNA-LNP formulations, including determining the potency and safety of the mRNA-LNPs for the delivery of therapeutic nucleic acid payloads. In collaboration with other scientists, Acuitas has elucidated the mechanism by which mRNA-LNPs are taken up by cells. Acuitas has also undertaken the biophysical characterization of such novel mRNA-LNPs and has conducted correlation analyses to determine which structural and biophysical properties of the components, including which structural and biophysical properties of the cationic lipids, are

critical for activity and safety. Acuitas has used this knowledge to guide subsequent lipid and mRNA-LNP development. This design and screening approach has allowed for the identification of mRNA-LNP formulations with greatly improved safety and efficacy profiles, including COMIRNATY®.

29. Acuitas is researching and will continue to research and collaborate with partners to develop drugs utilizing Acuitas LNP technology to combat difficult-to-treat conditions and provide novel methods of treatment for disease. This work, and the potential benefit of the Acuitas mRNA-LNP technology, goes far beyond a vaccine against the virus that causes COVID-19, notwithstanding the enormous success of COMIRNATY®.

COMIRNATY®

30. The origins of COMIRNATY® lie in collaborations between Acuitas and BioNTech that preceded the COVID-19 pandemic. In 2017, Acuitas and BioNTech began to collaborate on the development of mRNA therapeutic products using the Acuitas LNP technology. At or around the same time, Acuitas had also been collaborating with another German company, CureVac N.V. ("CureVac"), which in 2019 began a Phase 1 clinical trial of an mRNA vaccine against rabies, using Acuitas's LNP technology. In January 2020, CureVac released the results of this clinical trial, showing a strong immune response to the vaccine at a remarkably low dose. These very encouraging clinical data were released at the same time as the global threat from COVID-19 was becoming apparent. Acuitas therefore quickly engaged with CureVac and BioNTech to discuss use of the same LNP technology to develop an mRNA vaccine against COVID-19. The LNP used in the rabies vaccine contained the proprietary Acuitas lipids ALC-315 and ALC-159, and Acuitas recommended that the planned COVID-19 vaccine use the same LNP composition.

31. The development of COMIRNATY® itself began in January 2020, at the onset of the pandemic, when BioNTech started creating an mRNA molecule that codes for the "spike protein" of the COVID-19 SARS-CoV-2 coronavirus. BioNTech started working with Pfizer in March 2020 to develop and produce a COVID-19 vaccine. The rapid development of COMIRNATY® was possible in part because BioNTech had access to the Acuitas LNP technology, and had been collaborating with Acuitas on the use of that technology for several years. Further, Acuitas actively supported the formulation and evaluation of various COVID-19 vaccine candidates and worked with BioNTech and Pfizer to support scale-up of the manufacturing process to allow subsequent production of the billions of vaccine doses needed globally.

32. In May 2020, Pfizer and BioNTech initiated a Phase 1/2 clinical trial, which showed that healthy volunteers who took the vaccine could produce antibodies against the SARS-CoV-2 coronavirus and could recruit immune-system T cells that respond to, target, and destroy the SARS-CoV-2 coronavirus.

33. Phase 2/3 trials of COMIRNATY® began in July 2020, and were one of the two large studies of safety and efficacy of a COVID-19 vaccine in the United States. Pfizer and BioNTech's Phase 2/3 trials tested whether COMIRNATY® was efficacious in preventing COVID-19 infections and/or reducing the severity of COVID-19 infections. The results of the COMIRNATY® Phase 2/3 clinical trials were extremely promising, showing an efficacy rate of 95%.

34. While Phase 2/3 clinical trials were ongoing, the federal government recognized the importance of the vaccine and announced a $1.95 billion contract to purchase 100 million doses of COMIRNATY® in July of 2020 and announced another $1.95 billion contract for another 100

million doses of COMIRNATY® by December 2020, bringing the government's total purchase commitment to almost $4 billion.

35. On November 18, 2020, BioNTech and Pfizer announced that their COVID-19 vaccine met all the primary efficacy endpoints in their Phase 3 study, demonstrating an efficacy rate of 95% ($p < 0.0001$) in participants without prior SARS-CoV-2 infection (first primary objective) and also in participants with and without prior SARS-CoV-2 infection (second primary objective), as measured from 7 days after the second dose of the vaccine.

36. On December 11, 2020, COMIRNATY® was approved by the FDA under an Emergency Use Authorization to prevent COVID-19 in individuals 16 years of age and older. That EUA approval came less than ten months after BioNTech first created an mRNA molecule coding for the spike protein of the SARS-CoV-2 virus.

37. COMIRNATY® immediately started being deployed nationwide in vaccination efforts.

38. By summer 2021, the federal government and the European Union had negotiated deals with Pfizer and BioNTech to purchase billions of doses of COMIRNATY®.

39. On May 10, 2021, the FDA expanded the Emergency Use Authorization of COMIRNATY® to include children as young as 12. Later, on October 29, 2021, the Emergency Use Authorization was expanded to children as young as 5.

40. As a result of the safety profile and efficacy of COMIRNATY®, including information obtained as a result of the successful vaccination efforts during 2020 and early 2021, and in conjunction with further scientific studies, the FDA gave full approval of COMIRNATY® on August 23, 2021. COMIRNATY® was the first COVID-19 vaccine to receive such approval.

41. Following full approval, COMIRNATY® was found to be efficacious in combating not just the original COVID-19 strains but also the Beta, Delta, and Omicron variants that swept the world following the initial 2020 outbreak.

42. To date, Pfizer and BioNTech have delivered billions of doses of COMIRNATY® worldwide to combat the COVID-19 pandemic, all containing the lipids and lipid nanoparticles innovated by Acuitas that deliver this critical mRNA therapeutic.

Arbutus and Genevant

43. Arbutus's origins also began with the founders of Acuitas. In 1992, Acuitas founders Dr. Cullis, Dr. Madden, and Dr. Hope founded Arbutus's predecessor Inex (later rebranded as Tekmira). Dr. Cullis left Tekmira in 2005; Dr. Madden and Dr. Hope left Tekmira in 2008.

44. Although Arbutus, including its predecessors Inex, Protiva, and Tekmira, has worked on LNP technology, COMIRNATY® does not utilize lipids or LNP formulations developed by Genevant, Arbutus, or their shareholder Roivant. Neither Arbutus nor Genevant has a COVID-19 vaccine product competing against COMIRNATY® on the market nor, on information and belief, has either ever attempted to develop or commercialize an mRNA-based COVID-19 vaccine product.

45. Yet just days after BioNTech and Pfizer announced their positive Phase 3 COVID-19 vaccine results on November 18, 2020, on November 23, 2020, Genevant and Arbutus wrote a letter to Pfizer, stating: "We believe and notify you as contemplated by 35 U.S.C. § 287(a) that the manufacture, importation, offer for sale, sale, and/or use of your COVID-19 vaccine may infringe Arbutus patents, including at least U.S. Patent Nos. 8,058,069, 8,492,359, 8,822,668, 9,006,417, 9,404,127, 9,364,435, 9,504,651, and 9,518,272."

46. On October 12, 2021, Genevant and Arbutus wrote another letter to Pfizer, stating: "[W]e believe, and notify Pfizer and BioNTech under 35 U.S.C. § 287(a), that the manufacture, importation, offer for sale, sale, and/or use of the Pfizer-BioNTech COVID-19 vaccine Comirnaty® may infringe Arbutus['s] U.S. Patent No. 11,141,378, in addition to at least the Arbutus patents that were identified in our November 23, 2020 letter."

47. On information and belief, Genevant seeks hundreds of millions, if not billions, of dollars in unjustified royalties on sales of COMIRNATY®. That demand hinders the ability of Acuitas, as well as its partners such as BioNTech and Pfizer, to freely research, develop, and commercialize therapeutics utilizing Acuitas's LNP technology, including COVID-19 vaccines.

48. Arbutus's and Genevant's demands make it such that Acuitas and any company that works with Acuitas or utilizes Acuitas's LNPs or LNP technology face the risk of suit for infringement of one or more claims of the Arbutus Patents. Acuitas's business model is to develop LNP technology and license it to partners who will use the technology to develop mRNA-based vaccines and other therapeutic products. It is very important to Acuitas's business that partners and prospective partners can use the licensed Acuitas LNP technology free and clear of any third-party patents. Arbutus's and Genevant's demands thus impact the relationship between Acuitas and its current partners, including BioNTech and Pfizer, as well as Acuitas's ability to enter into new relationships with other potential partners.

49. Accordingly, Acuitas seeks a declaratory judgment that COMIRNATY® does not infringe any claim of the Arbutus Patents, and/or that each of the Arbutus Patents is invalid. Such a declaration of the rights of the parties is appropriate and necessary for Acuitas to continue providing its critical lipids and LNP formulations for the production of COMIRNATY® and for

Acuitas to freely conduct its LNP research and partner with entities to develop additional therapeutics.

THE PATENTS IN SUIT

U.S. Patent No. 8,058,069

50. On information and belief, Arbutus is the owner of all rights, title, and interest in the '069 patent, entitled "Lipid Formulations for Nucleic Acid Delivery." The United States Patent and Trademark Office issued the '069 patent on November 15, 2011. The '069 patent names Edward Yaworski, Kieu Lam, Lloyd Jeffs, Lorne Palmer, and Ian MacLachlan as inventors. All the named inventors assigned the '069 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the '069 patent is attached to this Complaint as Exhibit A.

51. The '069 patent contains one independent claim, claim 1, which claims a "nucleic acid-lipid particle comprising" "a nucleic acid," "a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid," "a non-cationic lipid comprising a mixture of a phospholipid and cholesterol or a derivative thereof," and "a conjugated lipid that inhibits aggregation of particles."

U.S. Patent No. 8,492,359

52. On information and belief, Arbutus is the owner of all rights, title, and interest in the '359 patent, entitled "Lipid Formulations for Nucleic Acid Delivery." The USPTO issued the '359 patent on July 23, 2013. The '359 patent names Edward Yaworski, Kieu Lam, Lloyd Jeffs, Lorne Palmer, and Ian MacLachlan as inventors. All the named inventors assigned the '359 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the '359 patent is attached to this Complaint as Exhibit B.

53. The '359 patent contains one independent claim, claim 1, which claims a "nucleic acid-lipid particle comprising" "a nucleic acid," "a cationic lipid comprising from 50 mol % to 65

mol % of the total lipid," "a non-cationic lipid comprising a mixture of a phospholipid and cholesterol or a derivative thereof," and "a conjugated lipid that inhibits aggregation of particles."

U.S. Patent No. 8,822,668

54. On information and belief, Arbutus is the owner of all rights, title, and interest in the '668 patent, entitled "Lipid Formulations for Nucleic Acid Delivery." The USPTO issued the '668 patent on September 2, 2014. The '668 patent names Edward Yaworski, Kieu Lam, Lloyd Jeffs, Lorne Palmer, and Ian MacLachlan as inventors. All the named inventors assigned the '668 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the '668 patent is attached to this Complaint as Exhibit C.

55. The '668 patent contains an independent claim, claim 1, that claims a "nucleic acid-lipid particle comprising" "a nucleic acid," "a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid," "a non-cationic lipid . . . comprising a mixture of a phospholipid and cholesterol or a derivative thereof," and "a conjugated lipid that inhibits aggregation of particles." Further, the '668 patent claims methods for "treating a disease or disorder" and "in vivo delivery of a nucleic acid" comprising the administration of the "nucleic acid-lipid particle" of claim 1.

U.S. Patent No. 9,006,417

56. On information and belief, Arbutus is the owner of all rights, title, and interest in the '417 patent, entitled "Non-Liposomal Systems for Nucleic Acid Delivery." The USPTO issued the '417 patent on April 14, 2015. The '417 patent names Edward Yaworski, Lloyd Jeffs, and Lorne Palmer as inventors. All the named inventors assigned the '417 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the '417 patent is attached to this Complaint as Exhibit D.

57. The ’417 patent contains an independent claim, claim 1, that claims a “composition comprising” “plurality of nucleic acid-lipid particles, wherein each particle . . . comprises” “a nucleic acid,” “a cationic lipid comprising from 50 mol % to 85 mol % of the total lipid,” “a non-cationic lipid,” and “a conjugated lipid that inhibits aggregation of particles” where “at least about 95% of the particles . . . have a non-lamellar morphology.” Further, the ’417 patent claims methods of “introducing a therapeutic agent into a cell” and “in vivo delivery of a therapeutic agent” comprising the composition claimed in claim 1.

U.S. Patent No. 9,364,435

58. On information and belief, Arbutus is the owner of all rights, title, and interest in the ’435 patent, entitled “Lipid Formulations for Nucleic Acid Delivery.” The USPTO issued the ’435 patent on June 14, 2016. The ’435 patent names Edward Yaworski, Kieu Lam, Lloyd Jeffs, Lorne Palmer, and Ian MacLachlan as inventors. All the named inventors assigned the ’435 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the ’435 patent is attached to this Complaint as Exhibit E.

59. The ’435 patent contains an independent claim, claim 1, that claims a “nucleic acid-lipid particle comprising” “a nucleic acid,” “a cationic lipid comprising from 50 mol % to 85 mol % of the total lipid,” “a non-cationic lipid,” and “a conjugated lipid that inhibits aggregation of particles.” Further, the ’435 patent claims methods of “introducing a nucleic acid into a cell,” “in vivo delivery of a nucleic acid,” and “treating a disease or disorder” comprising the nucleic acid-lipid particle claimed in claim 1.

U.S. Patent No. 9,404,127

60. On information and belief, Arbutus is the owner of all rights, title, and interest in the ’127 patent, entitled “Non-Liposomal Systems for Nucleic Acid Delivery.” The USPTO issued

the ’127 patent on August 2, 2016. The ’127 patent names Edward Yaworski, Lloyd Jeffs, and Lorne Palmer as inventors. All the named inventors assigned the ’127 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the ’127 patent is attached to this Complaint as Exhibit F.

61. The ’127 patent contains an independent claim, claim 1, that claims a “composition comprising” “a plurality of nucleic acid-lipid particles, wherein each particle . . . comprises” “a nucleic acid,” “a cationic lipid,” “a non-cationic lipid,” and “a conjugated lipid that inhibits aggregation of particles” where “at least about 95% of the particles . . . have a non-lamellar morphology.” Further, the ’127 patent claims methods of “introducing a therapeutic agent into a cell” and “in vivo delivery of a therapeutic agent” comprising the composition claimed in claim 1.

U.S. Patent No. 9,504,651

62. On information and belief, Arbutus is the owner of all rights, title, and interest in the ’651 patent, entitled “Lipid Compositions for Nucleic Acid Delivery.” The USPTO issued the ’651 patent on November 29, 2016. The ’651 patent names Ian MacLachlan, Lloyd Jeffs, Lorne Palmer, and Cory Giesbrecht as inventors. All the named inventors assigned the ’651 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the ’651 patent is attached to this Complaint as Exhibit G.

63. The ’651 patent contains one independent claim, claim 1, which claims a “lipid vesicle formulation comprising” “a plurality of lipid vesicles, wherein each lipid vesicle comprises” “a cationic lipid; an amphipathic lipid; and a polyethyleneglycol (PEG)-lipid” and a “messenger RNA.”

U.S. Patent No. 9,518,272

64. On information and belief, Arbutus is the owner of all rights, title, and interest in the '272 patent, entitled "Non-Liposomal Systems for Nucleic Acid Delivery." The USPTO issued the '272 patent on December 13, 2016. The '272 patent names Edward Yaworski, Lloyd Jeffs, and Lorne Palmer as inventors. All the named inventors assigned the '272 patent to Protiva, which subsequently amalgamated into Arbutus. A copy of the '272 patent is attached to this Complaint as Exhibit H.

65. The '272 patent contains an independent claim, claim 1, that claims a "composition comprising" "a plurality of nucleic acid-lipid particles, wherein each particle . . . comprises" "a nucleic acid," "a cationic lipid," "a non-cationic lipid," and "a conjugated lipid that inhibits aggregation of particles" where "at least 95% of the particles . . . are electron-dense." Further, the '272 patent claims methods of "introducing a therapeutic agent into a cell" and "in vivo delivery of a therapeutic agent" comprising the composition claimed in claim 1.

U.S. Patent No. 11,141,378

66. On information and belief, Arbutus is the owner of all rights, title, and interest in the '378 patent, entitled "Lipid Formulations for Nucleic Acid Delivery." The USPTO issued the '378 patent on October 12, 2021. The '378 patent names Edward Yaworski, Kieu Lam, Lloyd Jeffs, Lorne Palmer, and Ian MacLachlan as inventors. All the named inventors assigned the '378 patent to Arbutus. A copy of the '378 patent is attached to this Complaint as Exhibit I.

67. The '378 patent contains one independent claim, claim 1, which claims a "nucleic acid-lipid particle consisting essentially of" "an RNA," "a cationic lipid having a protonatable tertiary amine," "a mixture of a phospholipid and cholesterol," and "a polyethyleneglycol (PEG)-lipid conjugate."

COUNT I

(NON-INFRINGEMENT OF THE '127 PATENT)

68. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 67.

69. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '127 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, infringes any valid claim of the '127 patent.

70. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '127 patent.

71. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "nucleic acid-lipid particles" that comprise "a cationic lipid" as those terms are used in the '127 patent.

72. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '127 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '127 patent.

COUNT II

(INVALIDITY OF THE '127 PATENT)

73. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 72.

74. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of one or more claims of the '127 patent.

75. The claims of the '127 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

76. For example, the claims of the '127 patent are invalid as being anticipated under 35 U.S.C. § 102 by at least the '069 patent. That was the conclusion of the United States Patent Office in the Final Written Decision in an Inter Partes Review against that patent, IPR2018-00680. In addition, the claims of the '127 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art: the '069 patent; MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published Jun. 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); MacLachlan et al., WO 2009/082817 (published July 9, 2009); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

77. The claims of the '127 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe, or enable a person of ordinary skill in the art to make and use, a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

78. The claims of the '127 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '127 patent and which lipids constitute a "conjugated lipid that inhibits aggregation of particles" within the meaning of the '127 patent.

79. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable or have a non-lamellar morphology when the identity and amount of the nucleic acid and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Arbutus's arguments confirm that the claims of the '127 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

80. Acuitas hereby seeks a declaration that the claims of the '127 patent are invalid.

COUNT III

(NON-INFRINGEMENT OF THE '435 PATENT)

81. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 80.

82. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '435 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®,

or the importation of COMIRNATY® into the United States, infringes any valid claim of the '435 patent.

83. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '435 patent.

84. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "a cationic lipid comprising from 50 mol % to 85 mol % of the total lipid present in the particle" as required by the claims of the '435 patent.

85. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '435 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '435 patent.

COUNT IV

(INVALIDITY OF THE '435 PATENT)

86. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 85.

87. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of one or more claims of the '435 patent.

88. The claims of the '435 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

89. For example, the claims of the '435 patent are invalid as being anticipated by at least Chen et al., U.S. 2006/0240554 A1 (published Oct. 26, 2006). That was the conclusion of the United States Patent Office in the Final Written Decision in an Inter Partes Review, IPR2018-

00739, for certain claims of the '435 patent. In addition, the claims of the '435 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art: MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

90. The claims of the '435 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe, or enable a person of ordinary skill in the art to make and use, a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

91. The claims of the '435 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '435 patent and which lipids constitute a "conjugated lipid that inhibits aggregation of particles" within the meaning of the '435 patent.

92. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable when the identity and the amount of the nucleic acid and each of the claimed lipids

is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Arbutus's arguments confirm that the claims of the '435 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

93. Acuitas hereby seeks a declaration that the claims of the '435 patent are invalid.

COUNT V

(NON-INFRINGEMENT OF THE '069 PATENT)

94. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 93.

95. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '069 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, infringes any valid claim of the '069 patent.

96. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States does not infringe any valid claim of the '069 patent.

97. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle" as required by the claims of the '069 patent.

98. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '069 patent and that

the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '069 patent.

COUNT VI

(INVALIDITY OF THE '069 PATENT)

99. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 98.

100. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '069 patent.

101. The claims of the '069 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

102. For example, the claims of the '069 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '069 patent: MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

103. The claims of the '069 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe, or

enable a person of ordinary skill in the art to make and use, a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

104. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable when the identity and the amount of the nucleic acid and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such arguments confirm that the claims of the '069 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

105. The claims of the '069 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '069 patent and which lipids constitute a "conjugated lipid that inhibits aggregation of particles" within the meaning of the '069 patent.

106. Acuitas hereby seeks a declaration that the claims of the '069 patent are invalid.

COUNT VII

(NON-INFRINGEMENT OF THE '359 PATENT)

107. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 106.

108. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '359 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, infringes any valid claim of the '359 patent.

109. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States does not infringe any valid claim of the '359 patent.

110. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle" as required by the claims of the '359 patent.

111. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '359 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '359 patent.

COUNT VIII

(INVALIDITY OF THE '359 PATENT)

112. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 111.

113. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '359 patent.

114. The claims of the '359 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

115. For example, the claims of the '359 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '359 patent: MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

116. The claims of the '359 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe or enable a person of ordinary skill in the art to make and use a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

117. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable when the identity and the amount of the nucleic acid and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such arguments confirm that the claims of the '359 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

118. The claims of the ’359 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a “cationic lipid” within the meaning of the ’359 patent and which lipids constitute a “conjugated lipid that inhibits aggregation of particles” within the meaning of the ’359 patent.

119. Acuitas hereby seeks a declaration that the claims of the ’359 patent are invalid.

COUNT IX

(NON-INFRINGEMENT OF THE ’668 PATENT)

120. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 119.

121. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the ’668 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States infringes any valid claim of the ’668 patent.

122. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States does not infringe any valid claim of the ’668 patent.

123. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise “a cationic lipid comprising from 50 mol % to 65 mol % of the total lipid present in the particle” as required by the claims of the ’668 patent.

124. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the ’668 patent and that

the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '668 patent.

COUNT X

(INVALIDITY OF THE '668 PATENT)

125. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 124.

126. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '668 patent.

127. The claims of the '668 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

128. For example, the claims of the '668 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '668 patent: MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

129. The claims of the '668 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe or

enable a person of ordinary skill in the art to make and use a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

130. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable when the identity and the amount of the nucleic acid and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such arguments confirm that the claims of the '668 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

131. The claims of the '668 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '668 patent and which lipids constitute a "conjugated lipid that inhibits aggregation of particles" within the meaning of the '668 patent.

132. Acuitas hereby seeks a declaration that the claims of the '668 patent are invalid.

COUNT XI

(NON-INFRINGEMENT OF THE '417 PATENT)

133. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 132.

134. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '417 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States infringes any valid claim of the '417 patent.

135. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '417 patent.

136. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "a cationic lipid comprising from 50 mol % to 85 mol % of the total lipid present in the particle" as required by the claims of the '417 patent.

137. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '417 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '417 patent.

COUNT XII

(INVALIDITY OF THE '417 PATENT)

138. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 137.

139. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '417 patent.

140. The claims of the '417 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

141. For example, the claims of the '417 patent are invalid as being anticipated under 35 U.S.C. § 102 by at least the '069 patent as set forth in the Final Written Decision in IPR2018-00680. In addition, the claims of the '417 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '417 patent: the '069 patent; MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); MacLachlan et al., WO 2009/082817 (published July 9, 2009); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

142. The claims of the '417 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe or enable a person of ordinary skill in the art to make and use a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

143. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable or have a non-lamellar morphology when the identity and the amount of the nucleic acid and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such

arguments confirm that the claims of the '417 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

144. The claims of the '417 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '417 patent and which lipids constitute a "conjugated lipid that inhibits aggregation of particles" within the meaning of the '417 patent.

145. Acuitas hereby seeks a declaration that the claims of the '417 patent are invalid.

COUNT XIII

(NON-INFRINGEMENT OF THE '651 PATENT)

146. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 145.

147. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '651 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States infringes any valid claim of the '651 patent.

148. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '651 patent.

149. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "a cationic lipid" as required by the claims of the '651 patent.

150. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '651 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '651 patent.

COUNT XIV

(INVALIDITY OF THE '651 PATENT)

151. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 150.

152. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '651 patent.

153. The claims of the '651 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

154. For example, the claims of the '651 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '651 patent: Saravolac et al., U.S. Patent No. 6,734,171 (published May 11, 2004), Semple et al., WO 1998/051278 (published Nov. 19, 1998), and Semple et al., *Efficient Encapsulation of Antisense Oligonucleotides in Lipid Vesicles Using Ionizable Aminolipids: Formation of Novel Small Multilamellar Vesicle Structures*, 1510 Biochimica et Biophysica Acta 152 (2001).

155. The claims of the '651 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe or enable a person of ordinary skill in the art to make and use a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

156. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given lipid vesicle will be viable or fully encapsulate at least 70% of the mRNA in the formulation when the identity and the amount of mRNA and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such arguments confirm that the claims of the '651 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

157. The claims of the '651 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '651 patent.

158. Acuitas hereby seeks a declaration that the claims of the '651 patent are invalid.

COUNT XV

(NON-INFRINGEMENT OF THE '272 PATENT)

159. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 158.

160. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '272 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, infringes any valid claim of the '272 patent.

161. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '272 patent.

162. For example, the mRNA-LNP formulation in COMIRNATY® does not comprise "nucleic-acid lipid particles" that comprise "a cationic lipid" as those terms are used in the claims of the '272 patent.

163. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '272 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '272 patent.

COUNT XVI

(INVALIDITY OF THE '272 PATENT)

164. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 163.

165. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '272 patent.

166. The claims of the '272 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

167. For example, the claims of the '272 patent are invalid as being anticipated under 35 U.S.C. § 102 by at least the '069 patent for the same reasons as set forth in the Final Written Decision in IPR2018-00680 involving the '127 patent. In addition, the claims of the '272 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '272 patent: the '069 patent; MacLachlan et al., WO

2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); MacLachlan et al., WO 2009/082817 (published July 9, 2009); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

168. The claims of the '272 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe or enable a person of ordinary skill in the art to make and use a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in COMIRNATY®.

169. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable or be electron-dense when the identity and the amount of the nucleic acid and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such arguments confirm that the claims of the '272 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

170. The claims of the '272 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art

about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid" within the meaning of the '272 patent and which lipids constitute a "conjugated lipid that inhibits aggregation of particles" within the meaning of the '272 patent.

171. Acuitas hereby seeks a declaration that the claims of the '272 patent are invalid.

COUNT XVII

(NON-INFRINGEMENT OF THE '378 PATENT)

172. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 171.

173. There is an actual controversy between Acuitas and Arbutus and Genevant as to whether the mRNA-LNP formulation in COMIRNATY® meets all the limitations of any valid claim of the '378 patent and whether the manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, infringes any valid claim of the '378 patent.

174. The manufacture, use, offer to sell, or sale of COMIRNATY®, or the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '378 patent.

175. For example, the mRNA-LNP formulation in COMIRNATY® does not "consist[] essentially of" the claimed components, including "a cationic lipid having a protonatable tertiary amine," as required by the claims of the '378 patent.

176. Acuitas hereby seeks a declaration that the mRNA-LNP formulation in COMIRNATY® does not meet all of the limitations of any valid claim of the '378 patent and that the manufacture, use, offer to sell, and sale of COMIRNATY®, and the importation of COMIRNATY® into the United States, does not infringe any valid claim of the '378 patent.

COUNT XVIII

(INVALIDITY OF THE '378 PATENT)

177. Acuitas incorporates by reference herein all of the allegations of paragraphs 1 to 176.

178. There is an actual controversy between Acuitas and Arbutus and Genevant with respect to the validity of any claim of the '378 patent.

179. The claims of the '378 patent fail to meet one or more of the statutory requirements and/or conditions for patentability under the patent laws of the United States, including but not limited to 35 U.S.C. §§ 102-103, 112, *et seq*.

180. For example, the claims of the '378 patent are invalid as anticipated under 35 U.S.C. § 102 or rendered obvious under 35 U.S.C. § 103 by at least the following prior art to the '378 patent: MacLachlan et al., WO 2005/007196 (published Jan. 27, 2005); MacLachlan et al., U.S. Patent Publication No. 2006/0134189 A1 (published June 22, 2006); Lin et al., *Three-Dimensional Imaging of Lipid Gene-Carriers: Membrane Charge Density Controls Universal Transfection Behavior in Lamellar Cationic Liposome-DNA Complexes*, 84 Biophysical J. 3307-16 (2003); Ahmad et al., *New Multivalent Cationic Lipids Reveal Bell Curve for Transfection Efficiency Versus Membrane Charge Density: Lipid-DNA Complexes for Gene Delivery*, 7 J. Gene Med. 739-48 (2005); and Chen et al., U.S. Patent Publication No. 2006/0240554 A1 (published Oct. 26, 2006).

181. The claims of the '378 patent also are invalid for lack of written description and for lack of enablement pursuant to 35 U.S.C. § 112 because the specification does not describe or enable a person of ordinary skill in the art to make and use a formulation like Acuitas's mRNA-LNP formulations, including the mRNA-LNP formulation in the COMIRNATY®.

182. Further, Arbutus argued to the Patent Office, *e.g.*, in IPR2018-00739, IPR2018-00680, and IPR2019-00554, that it is unpredictable whether any given nucleic acid-lipid particle will be viable when the identity and the amount of the RNA and each of the claimed lipids is changed. For example, Arbutus argued: "The effects of making changes to the proportion of other components in the lipid particle would be unpredictable. Such changes, even if apparently minor in nature, would not be expected to produce a functional lipid particle suitable for systemic use." Patent Owner Response at 18, in IPR2018-00739. Such arguments confirm that the claims of the '378 patent are invalid for lack of written description, for lack of enablement, and for indefiniteness pursuant to 35 U.S.C. § 112.

183. The claims of the '378 patent are also invalid for indefiniteness pursuant to 35 U.S.C. § 112 as the specification fails to inform, with reasonable certainty, those of skill in the art about the scope of the invention. For example, the specification fails to inform, with reasonable certainty, which lipids constitute a "cationic lipid having a protonatable tertiary amine" within the meaning of the '378 patent.

184. Acuitas hereby seeks a declaration that the claims of the '378 patent are invalid.

PRAYER FOR RELIEF

WHEREFORE, Acuitas respectfully requests that this Court enter judgment in favor of Acuitas against Arbutus and Genevant and grant the following relief:

A. Judgment be entered declaring that the manufacture, use, offer to sell, and sale of COMIRNATY® in the United States, and the importation of COMIRNATY® into the United States, does not infringe any valid claims of any of the Arbutus Patents;

B. Judgment be entered declaring that all the claims of each of the Arbutus Patents are invalid;

C. Judgment be entered declaring this is an exceptional case and awarding Acuitas its attorneys' fees pursuant to 35 U.S.C. § 285;

D. Costs and expenses in this action; and

E. Such other and further relief as this Court may deem just and proper.

Respectfully submitted,

/s/ Nicholas Groombridge

PAUL, WEISS, RIFKIND, WHARTON & GARRISON LLP
Nicholas Groombridge
Eric Alan Stone
Josephine Young
Allison C. Penfield
1285 Avenue of the Americas
New York, NY 10019-6064
ngroombridge@paulweiss.com
estone@paulweiss.com
jyoung@paulweiss.com
apenfield@paulweiss.com
Telephone: (212) 373-3000
Facsimile: (212) 757-3990

Saurabh Gupta*
2001 K Street, NW
Washington, DC 20006-1047
sgupta@paulweiss.com
Telephone: (202) 223-7300
Facsimile: (202) 403-3157

Attorneys for Acuitas Therapeutics Inc.

**Pro hac vice application forthcoming*

Dated: March 18, 2022