IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

HARBOUR ANTIBODIES BV, HARBOUR ANTIBODIES HCAb BV, ERASMUS UNIVERSITY MEDICAL CENTER ROTTERDAM, DR. ROGER KINGDON CRAIG, *Plaintiffs*, v. TENEOBIO, INC., *Defendant*.	Case No.: **JURY TRIAL DEMANDED**

COMPLAINT AND DEMAND FOR JURY TRIAL
AND INJUNCTIVE RELIEF

Plaintiffs Harbour Antibodies BV ("HBV"), Harbour Antibodies HCAb BV ("HBAB") (together with HBV, the "Harbour Entities"), Erasmus University Medical Center Rotterdam ("Erasmus MC"), and Dr. Roger Kingdon Craig ("Craig") (collectively, "Plaintiffs") hereby assert the following claims for patent infringement against Defendant Teneobio, Inc. ("Defendant" or "Teneobio"), and allege as follows:

INTRODUCTION

1. Plaintiffs pioneered a novel method for developing fully human heavy chain-only antibodies (HCAbs) in rodents. Plaintiffs' patented platform technology utilizes transgenic rodents to generate functional HCAbs that can be used for therapeutic or research purposes. One embodiment of Plaintiffs' technology is the Harbour Mice®, which Plaintiffs created using its patented technology and which the Harbour Entities now utilize to generate and develop human therapeutic antibodies for itself and for its partners.

2. Plaintiffs invested significant time, effort, and money to develop the Harbour transgenic rodent platform technology, seeking patent protection on their inventions, raising venture capital to build up the business and platform, and partnering with pharmaceutical companies to utilize the patented technology. But after years of hard work, Plaintiffs' innovations were simply taken without permission by Defendant Teneobio.

3. In approximately 2015, Plaintiffs are informed and believe that Teneobio made a dramatic shift in its fledgling business plan and pivoted to HCAbs. Without any prior experience, Teneobio began developing an antibody discovery platform using transgenic rats, which it later called the UniRat®. Modeled after the Harbour Mice®, Teneobio's UniRat® discovery platform was developed for heavy chain only antibody production.[1] The UniRat® platform incorporates Plaintiffs' technology without Plaintiffs' permission and infringes the Asserted Patents (defined below).

4. Using Plaintiffs' patented technology, Teneobio has competed with the Harbour Entities for commercial partners and in the discovery and production of HCAbs. Teneobio has profited from the use of Plaintiffs' technology. Indeed, Teneobio has taken credit for the technology reflected in its UniRat® platform without ever recognizing the true origin of that technology as reflected in Plaintiffs' patents. Teneobio has been quite successful utilizing Plaintiffs' patented technology as most recently evidenced by Amgen, Inc.'s purchase of Teneobio and the UniRat® platform for more than $2.5 billion.[2]

[1] *See, e.g.*, Clarke, et al., "Multispecific Antibody Development Platform Based on Human Heavy Chain Antibodies." *Front. Immunol.*, 07 January 2019, attached hereto as Exhibit 5.
[2] https://www.amgen.com/newsroom/press-releases/2021/10/amgen-successfully-completes-acquisition-of-teneobio-inc.

5. As a result of Teneobio's infringement, Plaintiffs have suffered, and will continue to suffer, significant damages. This action is to remedy that infringement and to enforce Plaintiffs' patent rights against Teneobio.

NATURE OF THE ACTION

6. This is a civil action for patent infringement under the patent laws of the United States, 35 U.S.C. § 1, *et seq.*

7. Defendant has directly infringed and continues to infringe, has contributed to and continues to contribute to infringement of, and has induced and continues to induce infringement of one or more claims of U.S. Patent Nos. 9,346,877 (the "'877 Patent"), 9,353,179 (the "'179 Patent"), 10,906,970 (the "'970 Patent"), and 10,993,420 (the "'420 Patent") (collectively, the "Asserted Patents") through its development, use, and commercialization of the UniRat® platform and other actions.

8. As explained in more detail below, Plaintiffs are the legal owners and exclusive licensees of the Asserted Patents, which were duly and legally issued by the United States Patent and Trademark Office ("USPTO"). Plaintiffs seek injunctive relief and monetary damages.

THE PARTIES

9. Plaintiff HBAB is a corporation existing under the laws of the Netherlands, with its principal place of business at Groothandelsgebouw CIC Rotterdam, Stationsplein 45 unit A4.004, 3013 AK Rotterdam, The Netherlands.

10. Plaintiff HBV is a corporation existing under the laws of the Netherlands, with its principal place of business at Groothandelsgebouw CIC Rotterdam, Stationsplein 45 unit A4.004, 3013 AK Rotterdam, The Netherlands.

11. Plaintiff Erasmus MC is an academic medical center focused on patient care, education, and research and is located at Dr. Molewaterplein 50, 3015 GE Rotterdam, The Netherlands.

12. Plaintiff Craig is an individual who resides at Jubilee House Farm Spen Green, Smallwood, Sandbach, Cheshire, CW11 2XB, United Kingdom.

13. On information and belief, Defendant Teneobio is a corporation existing under the laws of the State of Delaware, with its principal place of business at 7999 Gateway Blvd., Suite 320, Newark, California 94560.

JURISDICTION AND VENUE

14. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331, 1332 and 1338(a) because this is a patent infringement action that arises under the patent laws of the United States, 35 U.S.C. § 1 *et seq.*

15. Defendant is subject to this Court's personal jurisdiction by virtue of the fact that Defendant is a corporation existing under the laws of the State of Delaware.

16. Venue is proper in this District under 28 U.S.C §§ 1391(b), (c), and/or 1400(b) because Defendant is incorporated in the State of Delaware, and therefore, resides in this judicial district.

ASSERTED PATENTS

17. This cause of action asserts infringement of the '877 Patent, the '179 Patent, the '970 Patent and the '420 Patent (collectively, the "Asserted Patents").

18. The USPTO rigorously scrutinizes applications related to biologics inventions, such as the inventions claimed in the Asserted Patents. That includes a strict examination to determine if the patent applications claim patent-eligible subject matter under 35 U.S.C. § 101.

Allowance rates for biologics-related inventions are low. The USPTO's allowance of patents in the biologics technology area thus reflects that the patents are valid and claim eligible subject matter.

19. A true and correct copy of the '877 Patent, entitled "Binding Molecules," with Franklin G. Grosveld, Richard W. Janssens, Dubravka Drabek, and Roger K. Craig as the named inventors, is attached hereto as Exhibit 1.

20. The '877 Patent duly and legally issued on May 24, 2016.

21. Erasmus MC and Craig are the current owners by assignment of all rights, title, and interest in and under the '877 Patent. HBV is the exclusive licensee of the '877 Patent and HBAB is the exclusive sub-licensee of the '877 Patent. Plaintiffs have standing to sue for infringement of the '877 Patent.

22. A true and correct copy of the '179 Patent, entitled "Binding Molecules," with Franklin G. Grosveld, Richard W. Janssens, Dubravka Drabek, and Roger K. Craig as the named inventors, is attached hereto as Exhibit 2.

23. The '179 Patent duly and legally issued on May 31, 2016.

24. Erasmus MC is the current owner by assignment of all rights, title, and interest in and under the '179 Patent. HBV is the exclusive licensee of the '179 Patent and HBAB is the exclusive sub-licensee of the '179 Patent. Plaintiffs have standing to sue for infringement of the '179 Patent.

25. A true and correct copy of the '970 Patent, entitled "Methods of Making Heavy Chain Only Antibodies Using Transgenic Animals," with Franklin G. Grosveld, Richard W. Janssens, Dubravka Drabek, and Roger K. Craig as the named inventors, is attached hereto as Exhibit 3.

26. The ’970 Patent duly and legally issued on February 2, 2021.

27. Erasmus MC and Craig are the current owners by assignment of all rights, title, and interest in and under the ’970 Patent. HBV is the exclusive licensee of the ’970 Patent and HBAB is the exclusive sub-licensee of the ’970 Patent. Plaintiffs have standing to sue for infringement of the ’970 Patent.

28. A true and correct copy of the ’420 Patent, entitled “Production of Heavy Chain Only Antibodies in Transgenic Mammals,” with Franklin G. Grosveld and Richard W. Janssens as the named inventors, is attached hereto as Exhibit 4.

29. The ’420 Patent duly and legally issued on May 4, 2021.

30. Erasmus MC is the owner by assignment of all rights, title, and interest in and under the ’420 Patent. HBV is the exclusive licensee of the ’420 Patent and HBAB is the exclusive sub-licensee of the ’420 Patent. Plaintiffs have standing to sue for infringement of the ’420 Patent.

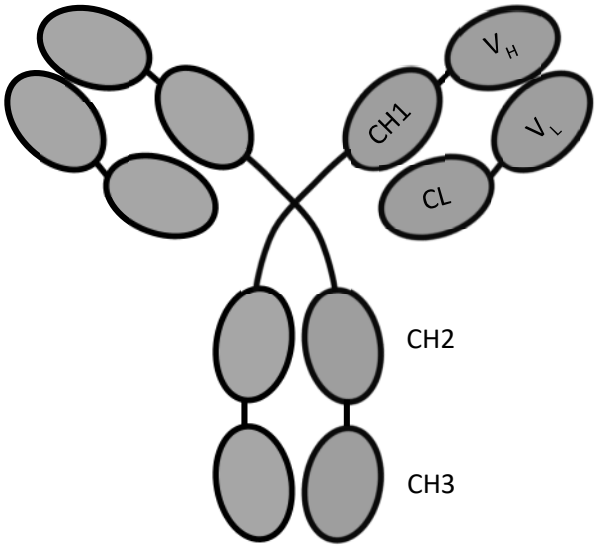
FACTUAL BACKGROUND

A. Heavy Chain-only Antibodies

31. An antibody is a protein produced by the immune system to identify and neutralize foreign pathogens such as bacteria, viruses, and even cancer cells. These target molecules are referred to as antigens. Each antibody recognizes and binds to a specific molecular structure on the surface of the antigen, also known as an epitope. Once the antibody binds to the antigen, it can trigger other components of the immune system to destroy the target molecule.

32. There are multiple classes of naturally occurring human antibodies, but all share a similar basic structure consisting of four polypeptide chains, as shown in the figure below. These four polypeptides are made up of two heavy chains and two light chains connected by disulfide bonds. Each chain is a series of domains: light chains consist of one variable domain (V_L) and one

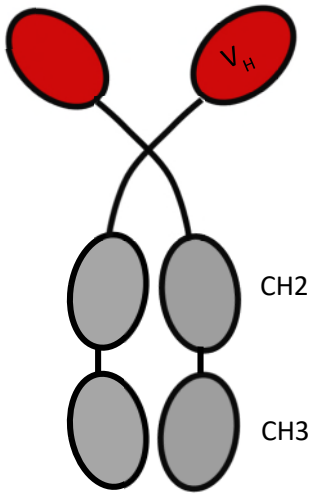
constant domain (C_L), while heavy chains contain one variable domain (V_H) and three to four constant domains (C_H1, C_H2, etc.). The variable regions of the heavy and light chain are responsible for recognizing and binding to a specific antigen. The tremendous variability in the antigen binding regions accounts for the enormous number of structurally distinct antigens that are recognized by antibodies.



Conventional
IgG antibody

33. Antibodies are generated by certain B cells that have been activated after coming into contact with an antigen. The activated B cell proliferates and differentiates into different types of B cells, including cells that secrete high-affinity antibodies.

34. HCAbs do not have associated light chains. As shown in the figure below, HCAbs contain heavy chain variable regions (V_H regions) and may contain heavy chain constant regions (C_H regions). The V_H regions function as a single domain. Without the associated light chains, HCAbs are highly functional and retain the ability to bind to antigen and present many advantages.



Heavy chain-only antibody

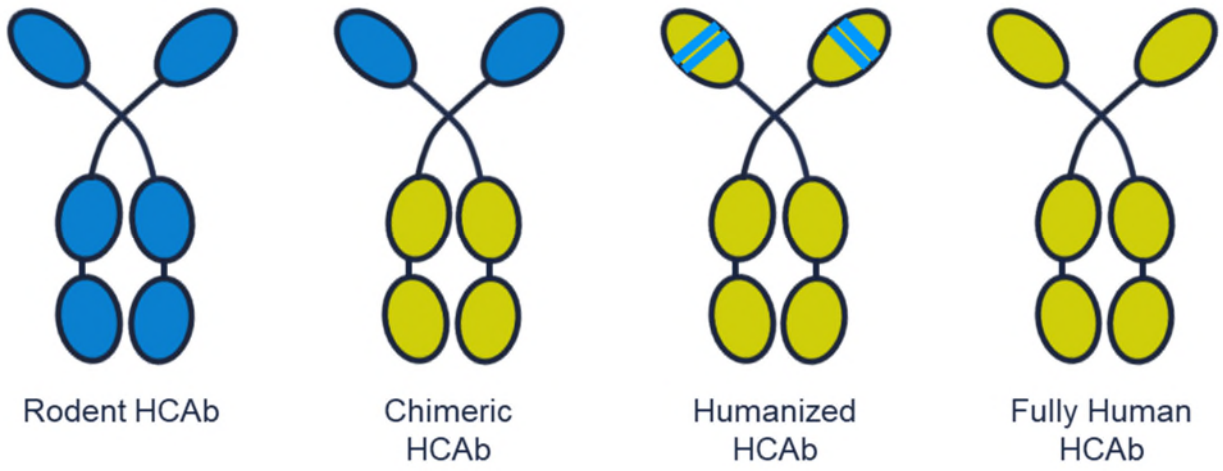
35. Monoclonal antibodies are specifically designed to bind to a particular epitope. Conventional or heavy chain-only monoclonal antibodies can be designed with monovalent affinity, binding only to single epitope, with bispecific affinity, binding simultaneously to epitopes on two different antigens or two different epitopes on one antigen, or with multispecific affinity, binding simultaneously with more than two epitopes.

36. Because monoclonal antibodies can be designed to bind to a specific target, they are useful as therapeutics, and in diagnostic and analytical tests. Because heavy chain-only antibodies are smaller in size and more suitable for designing bispecific or multi-specific antibodies, they can be designed to bind to epitopes that conventional monoclonal antibodies cannot access. Heavy chain-only antibodies also demonstrate strong antigen-binding affinity and are stable.

37. Heavy-chain only antibodies occur naturally in camels and cartilaginous fish, but not in humans. Because of the potential advantages that HCAbs have over conventional

antibodies, there was interest in the scientific community to develop a means for identifying and developing human HCAbs that could be engineered and used for therapeutic purposes.

38. Monoclonal HCAbs can be fully rodent, chimeric, humanized, or fully human. At a general level, a fully rodent antibody has no non-rodent protein sequences. Chimeric antibodies have a non-human variable region and human constant regions. A humanized antibody may have small segments of non-human sequences that are designed to be similar to human sequences and a fully human antibody has no non-human protein sequences. This general scheme is depicted in the image below.



B. Plaintiffs' Invent a Novel Method of Production of Human Heavy Chain-Only Antibodies

39. The Asserted Patents result from the inventive work of Franklin G. Grosveld, Richard W. Janssens, Dubravka Drabek, and Roger K. Craig over many years. Following the discovery of naturally occurring HCAbs in camels in the 1990s, the inventors embarked on a research plan to express recombinant porcine HCAbs in llamas to address the problem of porcine retroviruses in organs for potential use in xenotransplantation. After demonstrating the usefulness of HCAbs produced in llamas, the inventors shifted the focus of their work to develop a murine model that expressed human HCAbs.

40. Facing much skepticism in the field, the inventors spent years of laboratory work and solved numerous technical challenges to demonstrate that transgenic mice could produce HCAbs. For example, transgenic murine B cells express HCAbs at an early stage in B cell development, and the inventors first had to ensure that the murine B cells would grow and differentiate properly to produce HCAbs with the desired specificity. The inventors also had to ensure that the resulting HCAbs were sufficiently soluble to be functional.

41. These initial experiments were performed with HCAbs that incorporated llama V_H regions. The next step was to replace the llama V_H regions with human V_H regions to produce fully human HCAbs. While the inventors were ultimately successful, they faced overwhelming skepticism. Indeed, they had difficulty raising funds from venture capital sources or licensing partnerships as no one in the field believed the idea would work.

42. HBV was founded in 2006 to further develop and commercialize these discoveries and inventions. HBV was subsequently acquired by HBM Holdings Limited in 2016. HBM Holdings Limited ("HBM") was later listed in the Stock Exchange of Hong Kong Limited (stock code: 02142) in 2020. HBV, HBAB and other HBM subsidiaries are collectively called HBM Group.

43. HBAB was established in 2013 as a result of the demerger of HBV and was wholly owned by HBV with the goal of facilitating the licensing and commercialization of novel antibody therapeutics in the areas of oncology and immunological diseases.

44. HBAB, together with HBM Group, has since built a robust pipeline with its integrated Harbour antibody platform that enables it to develop highly differentiated antibodies against various disease targets with great potency and safety profiles. For example, HBAB's proprietary Harbour Mice® generates fully human monoclonal antibodies in the heavy chain only

(HCAb) format. Integrated with a single B cell cloning platform, HBAB's antibody discovery engine is highly unique and efficient for development of next generation therapeutic antibodies.

45. The claims of the Asserted Patents improve upon the conventional methods of producing antigen-specific HCAbs and offer a number of benefits, including the production of *in vivo*-derived HCAbs with critical quality attributes such as stability, solubility, and high affinity. Some of these benefits include:

a. The antibody formats produced by the Harbour Mice® have shown desirable expression yields and biophysical properties, such as solubility, non-aggregation and thermal stability, allowing for use either as simplified alternatives to conventional antibodies or as components of more complex antibody products.

b. The antibody formats produced by the Harbour Mice® have shown exceptional diversity from selected, frequently expressed and soluble human V-gene germline families. Immunized Harbour Mice® are able to yield non-identical, highly diverse collection of antibodies that recognize different epitopes, or binding regions, on the same target protein. Total variability of HCAb antibody panel can be increased simply by screening more antibodies from more immunized Harbour Mice®.

c. The HCAbs generated on the HCAb Platform have been observed to have a higher range of binding affinity (nanomolar to picomolar binders) which are significantly higher than those from competing technologies such as naive phage display libraries.

d. Due to the single chain nature of the HCAbs, they can be rapidly and deeply mined following immunization without the use of hybridoma technology, making them ready to progress very quickly into drug development. In addition, HBAB's fully human antibodies do not require any humanization, a process that at times has proven to be challenging and time consuming, and can result in antibodies with lowered binding affinities for their respective targets.

e. HCAbs have wide potential applications. When derived from the Harbour Mice®, the HCAbs are easily manipulated into making VH domain only molecules, bi-specifics or multi-specifics, VH domain-derived diagnostic or therapeutic molecules.[3]

[3] https://www.harbourbiomed.com/technology/1.html.

46. In short, Plaintiffs created a novel, elegant approach to producing antigen-specific HCAbs that can be used in next-generation therapeutic and diagnostic applications.

C. The Harbour Entities' Development Work, Partnerships and Licensees Have Been Damaged by Defendant's Infringement

47. The Harbour Entities' platforms have significant potential to generate therapeutic antibodies and accelerate drug discovery and development, which has been validated through more than 40 licenses to pharmaceutical and biotechnology companies as well as academic institutions.

48. On information and belief, Teneobio, Inc. is a clinical stage biotechnology company developing HCAbs for the treatments of cancer, autoimmunity, and infectious diseases.

49. On information and belief, Teneobio's discovery platform utilizes genetically engineered animals, including transgenic rats (*e.g.*, UniRat® and OmniFlic®), to identify large numbers of unique binding molecules specific for therapeutic targets of interest.

50. On information and belief, the UniRat® platform is based on immunization of transgenic rats that "result[s] in production of high affinity antigen-specific heavy chain only antibodies."[4]

51. On information and belief, Teneobio has licensed binding molecules, including heavy chain only antibodies, identified by its discovery platforms to several third parties.

52. On information and belief, Teneobio's UniRat® discovery platform [5] uses Plaintiff's inventions without Plaintiff's permission. It infringes the Asserted Patents.

[4] WO 2018/039180 A1 ("WO '180") (attached hereto as Exhibit 6), p. 22 lns. 26-27; *id*. at 23 lns 2-3.

[5] Teneobio's UniRat® multispecific antibody development platform based on human heavy chain antibodies, as accused of infringement in this case, includes the uses of the UniRat® in connection with any form of producing antigen-specific heavy chain only antibodies.

53. That Teneobio is commercializing an HCAb platform that infringes Plaintiffs' patents is not surprising. Teneobio has known of the inventors' work and the Asserted Patents well before Teneobio introduced its UniRat®. For example, Dr. Marianne Bruggemann, Ph.D., who is now associated with Teneobio, had meetings and discussions with the inventors concerning their patented technology as far back as 2005, and more recently sought access and license to the patented technology. Additionally, Teneobio's CEO, Dr. Roland Buelow, PhD, has attended numerous presentations by the inventors and has discussed the details of Plaintiffs' HCAb technology with them. Dr. Buelow expressed pessimism as to whether Plaintiffs' HCAb project would actually work.

D. Plaintiffs' Early Discussions With Defendant

54. The Harbour Entities, through their outside counsel, first contacted Teneobio's CEO, Dr. Roland Buelow, Ph.D., on October 6, 2017, to discuss Teneobio's infringement and possible resolution. In this initial communication, the Harbour Entities specifically identified the '877 and '179 patents as well as a corresponding European patent, and they identified Teneobio's work with human heavy chain only antibodies as potentially infringing. The Harbour Entities offered to engage in further discussions with Teneobio but Teneobio refused.

55. Instead, Teneobio's outside counsel responded on March 8, 2018. Defendant rejected the invitation to discuss potential licensing terms. Rather than engage in a productive discussion, Teneobio advanced an unsupported claim construction argument that allegedly absolved it of infringement liability (which it does not) and then baselessly threatened to seek sanctions should Plaintiffs seek legal redress.

56. Since then, Plaintiffs obtained two additional patents (namely, the '420 and '970 patents), both of which cover Teneobio's platform, products and activities. Undaunted by the Harbour Entities' notice, Teneobio has continued to tout Plaintiffs' patented technology as its own

and has deprived Plaintiffs of commercial opportunities – the latest of which was its sale to Amgen for more than $2.5 billion.

COUNT I
INFRINGEMENT OF THE U.S. PATENT NO. 9,346,877

57. The allegations of each foregoing paragraph are incorporated by reference as if fully set forth herein and from the basis for the following cause of action against Defendant.

58. Teneobio's activities, services, products (including Teneobio's UniAb™, UniDab™, TNB-383B, TNB-486 and TNB-585) and platform (including the design, function and use of the UniRat®) (collectively, the "Accused Methods and Products") are covered by at least claim 1 of the '877 Patent.

59. Claim 1 of the '877 Patent recites:

> A method for the production of soluble, antigen-specific V_H binding domain comprising:
> (a) immunising a transgenic rodent expressing a heterologous V_H heavy chain locus with an antigen wherein:
> (i) the V_H heavy chain locus comprises a variable region comprising at least one V_H gene segment, at least five D gene segment, at least one J gene segment and at least one heavy chain constant region;
> (ii) each constant region does not encode a functional C_H1 domain;
> (iii) a V_H gene segment, a D gene segment and a J gene segment are capable of recombining to form a VDJ coding sequence;
> (iv) the recombined V_H heavy chain locus, when expressed upon antigen challenge, is capable of forming a soluble, heavy chain-only antibody comprising a soluble, antigen-specific V_H binding domain and a constant effector region devoid of a functional C_Hl domain with an antigen;
> (b) cloning a V_H locus resulting from recombination between single V, D and J gene segments encoding a soluble, antigen-specific V_H binding domain from an antibody-producing cell of said immunised transgenic rodent after affinity maturation via somatic mutation; and
> (c) producing said soluble, V_H binding domain from the clone of step (b).

60. Defendant has infringed and continues to infringe, directly and/or under the doctrine of equivalents, at least claim 1 of the '877 Patent in violation of 35 U.S.C. § 271(a) by, directly or through intermediaries and without Plaintiff's authority, making, using, selling, and/or offering to sell the Accused Methods and Products in the United States.

61. By way of illustration and not as a limitation to the full scope of its infringing activities, Teneobio infringes claim 1 of the '877 Patent by having designed and used the UniRat® discovery platform to produce antigen-specific heavy chain only antibodies as follows:

(a) Teneobio uses the UniRat® discovery platform for the production of soluble, antigen-specific V_H binding domain. For example, the UniRat® platform is based on immunization of transgenic rats which "result[s] in production of high affinity antigen-specific heavy chain only antibodies."[6]

(b) The UniRat® discovery platform produces antigen-specific heavy chain only antibodies by immunizing a transgenic rodent expressing a heterologous V_H heavy chain locus with an antigen. For example, the UniRat® discovery platform is based on "genetically engineered rats expressing heavy chain only antibodies [that are] immunized in various ways."[7] The "UniRat . . . animals were immunized using standard adjuvants along with recombinant protein antigens."[8] Teneobio's UniRats "produce chimeric HCAbs with fully human VH domains in response to an antigen challenge."[9]

(c) In Teneobio's approach, the V_H heavy chain locus comprises a variable region comprising at least one V_H gene segment, at least five D gene segments, at least one J gene segment and at least one heavy chain constant region. For example, the UniRat® discovery platform also "concerns a recombinant heavy chain-only immunoglobulin (Ig) locus comprising one or more human V gene segments, one or more human D gene segments, and one or more human J gene segments." The platform's IG locus is made up of "two to 40 D gene segments," and the Ig locus "further comprises a constant (C) region gene segment, encoding an

[6] WO '180, p. 22 lns. 26-27; *id*. at 23 lns. 2-3.
[7] *Id*.
[8] *Clarke, et al.*, at 10.
[9] *Id*. at Abstract.

immunoglobulin constant effector region lacking CH1 functionality."[10] In "[c]onstruction of UniRat Strains . . . [l]arge IgH loci on BACs carrying human VH, D and JH segments in germline configuration linked to rat Cγ genes were compiled as detailed previously . . . except that a new assembly of rat CH genes lacking CH1 domains was used."[11]

(d) The constant regions in Teneobio's UniRat discovery platform do not encode a functional C_H1 domain. For example, "[c]onstruction of UniRat Strains . . . [l]arge IgH loci on BACs carrying human VH, D and JH segments in germline configuration linked to rat Cγ genes were compiled as detailed previously . . . except that a new assembly of rat CH genes lacking CH1 domains was used."[12] The UniRats® "lack all endogenous Ig expression and efficiently produce chimeric human/rat IgH molecules containing human VH, D, and JH sequences on rat constant regions deleted for CH1."[13] The "UniAbs [Teneobio's term for heavy chain only antibodies with fully human variable domains] lack CH1 domains and light chains, resulting in a molecular weight of approximately 80 kDa."[14]

(e) A V_H gene segment, a D gene segment and a J gene segment are capable of recombining to form a VDJ coding sequence. For example, the V gene segment of the UniRat® "must be capable of recombining with a D gene segment, a J gene segment and a heavy chain constant region, which excludes a CH1 exon, to generate a heavy chain-only antibody."[15]

(f) The recombined V_H heavy chain locus, when expressed upon an antigen challenge, is capable of forming a soluble, heavy chain-only antibody comprising a soluble, antigen-specific V_H binding domain and a constant effector region devoid of a functional C_H1

[10] WO '180 at p. 5, lns. 16-19; *id*. at p. 5, lns. 26-27; *id*. p. 5, lns. 24-25.
[11] *Clarke, et al.*, at p. 2.
[12] *Id*. at p. 2.
[13] *Id.* at p. 7.
[14] *Id*. at Fig. 1.
[15] WO '180 at p. 11, ln. 36 - p. 12, ln 2.

domain with an antigen. For example, the V gene segment of the UniRat® "must be capable of recombining with a D gene segment, a J gene segment and a heavy chain constant region, which excludes a CH1 exon, to generate a heavy chain-only antibody."[16] As part of the UniRat® discovery platform, "the recombinant heavy chain-only Ig locus further comprises a constant (C) region gene segment, encoding an immunoglobulin constant effector region lacking CH1 functionality."[17] "The term 'heavy chain-only locus' as defined [by the UniRat® discovery platform] refers to a locus encoding a VH domain in which the first amino acid residue of the antibody FR4 region is positively charged, comprising one or more V gene segments, one or more D gene segment and one or more J gene segments, optionally linked to one or more heavy chain effector region gene segments, each of which encodes an antibody constant effector region lacking CH1 domain functionality."[18]

(g) The UniRat® discovery platform clones a V_H locus resulting from recombination between single V, D and J gene segments encoding a soluble antigen-specific V_H binding domain from an antibody-producing cell of the immunized transgenic rodent after affinity maturation via somatic mutation. For example, the UniRat® discovery platform clones the V_H heavy chain locus after affinity maturation via somatic mutation: "Heavy chain only antibodies, including their VHH or VH functional fragments, can also be produced by recombinant DNA technology, by expression of the encoding nucleic acid in a suitable eukaryotic or prokaryotic host, including E. coli or yeast."[19] This cloning process happens after affinity maturation via somatic mutation: "[T]he invention concerns a recombinant heavy chain-only immunoglobulin (Ig) locus comprising one or more human V gene segments, one or more human D gene segments, and one

[16] *Id.*
[17] WO '180 at p. 5, lns. 24-25.
[18] *Id.* at p. 11, lns. 20-24.
[19] *Id.* at p. 14, lns. 7-10.

or more human J gene segments, which when recombined with each other in the genome of a non-human animal, and following affinity maturation, encode a heavy chain variable (VH) region."[20]

(h) From the cloning step, the UniRat® discovery platform produces a soluble, antigen-specific heavy chain only antibody. For example, "[h]eavy chain only antibodies, including their VHH or VH functional fragments, can also be produced by recombinant DNA technology, by expression of the encoding nucleic acid in a suitable eukaryotic or prokaryotic host, including E. coli or yeast."[21] Antibodies can be harvested from the discovery platform after several days of expression.[22]

62. Further and in the alternative, Defendant has been actively inducing infringement of at least claim 1 of the '877 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Methods and Products directly infringed at least claim 1 of the '877 Patent when they use the Accused Methods and Products in the ordinary, customary, and intended way as set forth in Teneobio's publications, which include but are not limited to those cited above. Defendant's inducements included, without limitation and with specific intent to encourage the infringement, knowingly inducing consumers to use the Accused Methods and Products within the United States in the ordinary, customary, and intended way by, directly or through intermediaries, supplying the Accused Methods and Products to consumers within the United States and instructing and encouraging such customers (for example, by offering the UniRat® discovery platform) how to use the Accused Methods and Products in the ordinary, customary, and intended way, which Defendant knows or should know infringes at least claim 1 of the '877 Patent.

[20] *Id.* at p. 5, lns. 16-19.
[21] WO '180 at p. 14, lns. 7-10.
[22] *Clarke, et al.*, at 10.

63. Defendant's inducements may further include, without limitation and with specific intent to encourage the infringement, knowingly inducing customers to use the Accused Methods and Products within the United States, or knowingly inducing customers to use the Accused Methods and Products within the United States, by, directly or through intermediaries, instructing and encouraging such customers to make, use, sell, or offer to sell the Accused Methods and Products in the United States, which Defendant knows or should know infringes at least claim1 of the '877 Patent.

64. Further and in the alternative, Defendant has been actively contributing to infringement of at least claim 1 of the '877 Patent in violation of 35 U.S.C. § 271(c). Defendant has offered for sale the UniRat®, which is especially made or especially adapted to practice the invention claimed in at least claim 1 of the '877 Patent. The UniRat® constitutes a material part of the claimed invention recited in at least claim 1 of the '877 Patent and is not a staple article or commodity of commerce because it is specifically configured according to at least claim 1 of the '877 Patent. Defendant's contributions include, without limitation, making, offering to sell, and/or selling within the United States, and/or importing into the United States, the Accused Methods and Products, which includes one or more components for use in practicing the patented process, knowing the component to be especially made or especially adapted for use in an infringement of at least claim 1 of the '877 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

65. Since October 6, 2017, Defendant has had actual knowledge of the '877 Patent and should have known of the '877 Patent well before then but for Teneobio's willful blindness. By the time this matter is adjudicated, Defendant will have known about the '877 Patent for years and intended that its continued actions since receiving such notice would infringe and actively induce

and contribute to the infringement of one or more claims of the '877 Patent. Defendant's infringement of the '877 Patent has been willful and deliberate.

66. Defendant's infringement has caused past and will cause ongoing injury to Plaintiffs. Plaintiffs are entitled to recover damages adequate to compensate for Defendant's infringement. Because Defendant's infringement has been and continues to be willful and deliberate, the Court should award enhanced damages under 35 U.S.C. § 284 and find this case exceptional and award attorney's fees under 35 U.S.C. § 285.

67. Plaintiffs have suffered and will continue to suffer irreparable injury as a direct and proximate result of Defendant's infringement for which there is no adequate remedy at law. Unless Defendant is enjoined, Plaintiffs will continue to suffer such irreparable injury.

68. Defendant's infringement has been without authority and/or license from Plaintiffs.

COUNT II
INFRINGEMENT OF THE U.S. PATENT NO. 9,353,179

69. The allegations of each foregoing paragraph are incorporated by reference as if fully set forth herein and from the basis for the following cause of action against Defendant.

70. The Accused Methods and Products are covered by at least claim 1 of the '179 Patent.

71. Claim 1 of the '179 Patent recites:

> A method for the production of soluble, antigen-specific heavy chain only antibodies comprising:
> (a) immunising a transgenic rodent expressing a heterologous V_H heavy chain locus with an antigen wherein:
> (i) the V_H heavy chain locus comprises a variable region comprising at least one V_H gene segment, at least five D gene segments, at least one J gene segment and at least one heavy chain constant region;
> (ii) each constant region does not encode a functional C_H1 domain;
> (iii) a V_H gene segment, a D gene segment and a J gene segment are capable of recombining to form a VDJ coding sequence;
> (iv) the recombined V_H heavy chain locus, when expressed upon antigen challenge, is capable of forming a soluble, heavy chain-only antibody

> comprising a soluble, antigen-specific V_H binding domain and a constant effector region devoid of a functional C_Hl domain with an antigen;
> (b) cloning a soluble heavy chain only antibody from an antibody-producing cell of said immunised transgenic rodent after affinity maturation via somatic mutation; ad
> (c) producing said soluble, antigen specific heavy chain only antibody from the clone of step (b).

72. Defendant has infringed and continues to infringe, directly and/or under the doctrine of equivalents, at least claim 1 of the '179 Patent in violation of 35 U.S.C. § 271(a) by, directly or through intermediaries and without HBAB's authority, making, using, selling, and/or offering to sell the Accused Methods and Products in the United States.

73. By way of illustration and not as a limitation to the full scope of its infringing activities, Teneobio infringes claim 1 of the '179 Patent by having designed and used the UniRat® discovery platform to produce antigen-specific heavy chain only antibodies as follows:

(a) Teneobio uses the UniRat® discovery platform for the production of soluble, antigen-specific heavy chain only antibodies. For example, the UniRat® platform is based on immunization of transgenic rats which "result[s] in production of high affinity antigen-specific heavy chain only antibodies."[23]

(b) The UniRat® discovery platform produces antigen-specific heavy chain only antibodies by immunizing a transgenic rodent expressing a heterologous V_H heavy chain locus with an antigen. For example, the UniRat® discovery platform is based on "genetically engineered rats expressing heavy chain only antibodies [that are] immunized in various ways."[24] The "UniRat… animals were immunized using standard adjuvants along with recombinant protein

[23] WO '180, p. 22 lns. 26-27; *id*. at 23 lns 2-3.
[24] *Id*.

antigens."[25] Teneobio's UniRats "produce chimeric HCAbs with fully human VH domains in response to an antigen challenge."[26]

(c) In Teneobio's approach, the V_H heavy chain locus comprises a variable region comprising at least one V_H gene segment, at least five D gene segments, at least one J gene segment and at least one heavy chain constant region. For example, the UniRat® discovery platform also "concerns a recombinant heavy chain-only immunoglobulin (Ig) locus comprising one or more human V gene segments, one or more human D gene segments, and one or more human J gene segments." The platform's IG locus is made up of "two to 40 D gene segments," and the Ig locus "further comprises a constant (C) region gene segment, encoding an immunoglobulin constant effector region lacking CH1 functionality."[27] In "[c]onstruction of UniRat Strains . . . [l] arge IgH loci on BACs carrying human VH, D and JH segments in germline configuration linked to rat Cγ genes were compiled as detailed previously (29, 31), except that a new assembly of rat CH genes lacking CH1 domains was used."[28]

(d) The constant regions in Teneobio's UniRat discovery platform do not encode a functional C_H1 domain. For example, "[c]onstruction of UniRat Strains . . . [l] arge IgH loci on BACs carrying human VH, D and JH segments in germline configuration linked to rat Cγ genes were compiled as detailed previously . . . except that a new assembly of rat CH genes lacking CH1 domains was used."[29] The UniRats® "lack all endogenous Ig expression and efficiently produce chimeric human/rat IgH molecules containing human VH, D, and JH sequences on rat constant regions deleted for CH1."[30] The "UniAbs [Teneobio's term for heavy chain only

[25] *Clarke, et al.*, at 10.
[26] *Id*. at Abstract.
[27] WO '180 at p. 5, lns. 16-19; *id*. at p. 5, lns. 26-27; *id*. p. 5, lns. 24-25.
[28] *Clarke, et al.*, at p. 2.
[29] *Id*. at p. 2.
[30] *Id* at p. 7.

antibodies with fully human variable domains] lack CH1 domains and light chains, resulting in a molecular weight of approximately 80 kDa."[31]

(e) A V_H gene segment, a D gene segment and a J gene segment are capable of recombining to form a VDJ coding sequence. For example, the V gene segment of the UniRat® "must be capable of recombining with a D gene segment, a J gene segment and a heavy chain constant region, which excludes a CH1 exon, to generate a heavy chain-only antibody."[32]

(f) The recombined V_H heavy chain locus, when expressed upon an antigen challenge, is capable of forming a soluble, heavy chain-only antibody comprising a soluble, antigen-specific V_H binding domain and a constant effector region devoid of a functional C_H1 domain with an antigen. For example, the V gene segment of the UniRat® "must be capable of recombining with a D gene segment, a J gene segment and a heavy chain constant region, which excludes a CH1 exon, to generate a heavy chain-only antibody."[33] As part of the UniRat® discovery platform, "the recombinant heavy chain-only Ig locus further comprises a constant (C) region gene segment, encoding an immunoglobulin constant effector region lacking CH1 functionality."[34] "The term 'heavy chain-only locus' as defined [by the UniRat® discovery platform] refers to a locus encoding a VH domain in which the first amino acid residue of the antibody FR4 region is positively charged, comprising one or more V gene segments, one or more D gene segment and one or more J gene segments, optionally linked to one or more heavy chain effector region gene segments, each of which encodes an antibody constant effector region lacking CH1 domain functionality."[35]

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[31] *Id*. at Fig. 1.
[32] WO '180 at p. 11, ln. 36 - p. 12, ln 2.
[33] *Id*.
[34] WO '180 at p. 5, lns. 24-25.
[35] *Id*. at p. 11, lns. 20-24.

(g) The UniRat® discovery platform then clones a soluble heavy chain only antibody from an antibody-producing cell of the immunized transgenic rodent after affinity maturation via somatic mutation. For example, the UniRat® discovery platform clones the V_H heavy chain locus after affinity maturation via somatic mutation: "Heavy chain only antibodies, including their VHH or VH functional fragments, can also be produced by recombinant DNA technology, by expression of the encoding nucleic acid in a suitable eukaryotic or prokaryotic host, including E. coli or yeast."[36] This cloning process happens after affinity maturation via somatic mutation: "[T]he invention concerns a recombinant heavy chain-only immunoglobulin (Ig) locus comprising one or more human V gene segments, one or more human D gene segments, and one or more human J gene segments, which when recombined with each other in the genome of a non-human animal, and following affinity maturation, encode a heavy chain variable (VH) region."[37]

(h) From the cloning step, the UniRat® discovery platform produces a soluble, antigen-specific heavy chain only antibody. For example, "[h]eavy chain only antibodies, including their VHH or VH functional fragments, can also be produced by recombinant DNA technology, by expression of the encoding nucleic acid in a suitable eukaryotic or prokaryotic host, including E. coli or yeast."[38] Antibodies can be harvested from the discovery platform after several days of expression.[39]

74. Further and in the alternative, Defendant has been actively inducing infringement of at least claim 1 of the '179 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Methods and Products directly infringed at least claim 1 of the '179 Patent when they use the Accused Methods and Products in the ordinary, customary, and intended way as set forth in

[36] *Id*. at p. 14, lns. 7-10.
[37] *Id*. at p. 5, lns. 16-19.
[38] WO '180 at p. 14, lns. 7-10.
[39] *Clarke, et al.*, at 10.

Teneobio's publications, which include but are not limited to those cited above. Defendant's inducements included, without limitation and with specific intent to encourage the infringement, knowingly inducing consumers to use the Accused Methods and Products within the United States in the ordinary, customary, and intended way by, directly or through intermediaries, supplying the Accused Methods and Products to consumers within the United States and instructing and encouraging such customers (for example, by offering the UniRat® discovery platform) how to use the Accused Methods and Products in the ordinary, customary, and intended way, which Defendant knows or should know infringes at least claim 1 of the '179 Patent.

75. Defendant's inducements may further include, without limitation and with specific intent to encourage the infringement, knowingly inducing customers to use the Accused Methods and Products within the United States, or knowingly inducing customers to use the Accused Methods and Products within the United States, by, directly or through intermediaries, instructing and encouraging such customers to make, use, sell, or offer to sell the Accused Methods and Products in the United States, which Defendant knows or should know infringes at least claim1 of the '179 Patent.

76. Further and in the alternative, Defendant has been actively contributing to infringement of at least claim 1 of the '179 Patent in violation of 35 U.S.C. § 271(c). Defendant has offered for sale the UniRat®, which is especially made or especially adapted to practice the invention claimed in at least claim 1 of the '179 Patent. The UniRat® constitutes a material part of the claimed invention recited in at least claim 1 of the '179 Patent and is not a staple article or commodity of commerce because it is specifically configured according to at least claim 1 of the '179 Patent. Defendant's contributions include, without limitation, making, offering to sell, and/or selling within the United States, and/or importing into the United States, the Accused Methods and

Products, which includes one or more components for use in practicing the patented process, knowing the component to be especially made or especially adapted for use in an infringement of at least claim 1 of the ’179 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

77. Since October 6, 2017, Defendant has had actual knowledge of the ’179 Patent and should have known of the ’179 Patent well before then but for Teneobio’s willful blindness. By the time this matter is adjudicated, Defendant will have known about the ’179 Patent for years and intended that its continued actions since receiving such notice would infringe and actively induce and contribute to the infringement of one or more claims of the ’179 Patent. Defendant’s infringement of the ’877 Patent has been willful and deliberate.

78. Defendant’s infringement has caused past and will cause ongoing injury to Plaintiffs. Plaintiffs are entitled to recover damages adequate to compensate for Defendant’s infringement. Because Defendant’s infringement has been and continues to be willful and deliberate, the Court should award enhanced damages under 35 U.S.C. § 284 and find this case exceptional and award attorney’s fees under 35 U.S.C. § 285.

79. Plaintiffs have suffered and will continue to suffer irreparable injury as a direct and proximate result of Defendant’s infringement for which there is no adequate remedy at law. Unless Defendant is enjoined, Plaintiffs will continue to suffer such irreparable injury.

80. Defendant’s infringement has been without authority and/or license from Plaintiffs.

COUNT III
INFRINGEMENT OF THE U.S. PATENT NO. 10,906,970

81. The allegations of each foregoing paragraph are incorporated by reference as if fully set forth herein and from the basis for the following cause of action against Defendant.

82. The Accused Methods and Products are covered by at least claim 1 of the '970 Patent.

83. Claim 1 of the '970 Patent recites:

> A method for the production of soluble, antigen-specific heavy chain only antibodies comprising:
> (a) immunising a transgenic rodent expressing a heterologous VH heavy chain locus with an antigen wherein:
> (i) the VH heavy chain locus comprises a variable region comprising at least one VH gene segment, from 20 to 40 D gene segments, at least one J gene segment and a heavy chain constant region comprising at least one constant region gene that does not encode a functional CH1 domain;
> (ii) a VH gene segment, a D gene segment and a J gene segment are capable of recombining to form a VDJ coding sequence;
> (iii) the recombined VH heavy chain locus, when expressed upon antigen challenge, is capable of forming a soluble, heavy chain-only antibody comprising a soluble, antigen-specific VH binding domain and a constant effector region devoid of a functional CH1 domain;
> (b) cloning said recombined VH heavy chain locus from an antibody-producing cell of said immunised transgenic rodent after affinity maturation via somatic mutation; and
> (c) producing said soluble, antigen specific heavy chain only antibody from the clone of step (b).

84. Defendant has infringed and continues to infringe, directly and/or under the doctrine of equivalents, at least claim 1 of the '970 Patent in violation of 35 U.S.C. § 271(a) by, directly or through intermediaries and without Plaintiffs' authority, making, using, selling, and/or offering to sell the Accused Methods and Products in the United States.

85. By way of illustration and not as a limitation to the full scope of its infringing activities, Teneobio infringes claim 1 of the '970 Patent by having designed and used the UniRat® discovery platform to produce antigen-specific heavy chain only antibodies as follows:

(a) The UniRat® platform is based on immunization of transgenic rats which "result[s] in production of high affinity antigen-specific heavy chain only antibodies."[40]

[40] WO '180, p. 22 lns. 26-27; *id*. at 23 lns 2-3.

(b) The UniRat® discovery platform produces antigen-specific heavy chain only antibodies by immunizing a transgenic rodent expressing a heterologous V_H heavy chain locus with an antigen. For example, in the UniRat® discovery platform, the "recombinant heavy chain-only Ig locus encodes a human or humanized heavy chain-only antibody comprising a VH region." [41] The UniRat® animals are "immunized using standard adjuvants along with recombinant protein antigens."[42]

(c) The UniRat's® V_H heavy chain locus is a variable region that consists of at least one V_H gene segment, from 20 to 40 D gene segments, at least one J gene segment, and a heavy chain constant region that has at least one constant region gene that does not encode a functional C_H1 domain. For example, the UniRat® discovery platform "concerns a recombinant heavy chain-only immunoglobulin (Ig) locus comprising one or more human V gene segments, one or more human D gene segments, and one or more human J gene segments." The platform's IG locus is made up of "two to 40 D gene segments," and the Ig locus "further comprises a constant (C) region gene segment, encoding an immunoglobulin constant effector region lacking CH1 functionality." [43] In "[c]onstruction of UniRat Strains . . . [l]arge IgH loci on BACs carrying human VH, D and JH segments in germline configuration linked to rat Cγ genes were compiled as detailed previously . . . except that a new assembly of rat CH genes lacking CH1 domains was used."[44]

(d) A V_H gene segment, a D gene segment and a J gene segment are capable of recombining to form a VDJ coding sequence. For example, the V gene segment of the UniRat®

[41] *Id*. at p. 6 lns. 7-10.
[42] *Clarke, et al*. at 2.
[43] WO '180 at p. 5, lns. 16-19; *id*. at p. 5, lns. 26-27; *id*. p. 5, lns. 24-25.
[44] *Clarke, et al.*, at p. 2.

"must be capable of recombining with a D gene segment, a J gene segment and a heavy chain constant region, which excludes a CH1 exon, to generate a heavy chain-only antibody."[45]

(e) The recombined V_H heavy chain locus, when expressed upon an antigen challenge, is capable of forming a soluble, heavy chain-only antibody comprising a soluble, antigen-specific V_H binding domain and a constant effector region devoid of a functional C_H1 domain. For example, the V gene segment of the UniRat® "must be capable of recombining with a D gene segment, a J gene segment and a heavy chain constant region, which excludes a CH1 exon, to generate a heavy chain-only antibody."[46] As part of the UniRat® discovery platform, "the recombinant heavy chain-only Ig locus further comprises a constant (C) region gene segment, encoding an immunoglobulin constant effector region lacking CH1 functionality."[47] "The term 'heavy chain-only locus' as defined [by the UniRat® discovery platform] refers to a locus encoding a VH domain in which the first amino acid residue of the antibody FR4 region is positively charged, comprising one or more V gene segments, one or more D gene segment and one or more J gene segments, optionally linked to one or more heavy chain effector region gene segments, each of which encodes an antibody constant effector region lacking CH1 domain functionality."[48]

(f) The UniRat® discovery platform recombines V_H heavy chain locus from an antibody-producing cell of the immunized transgenic rodent after affinity maturation via somatic mutation. For example, the UniRat® discovery platform clones the V_H heavy chain locus after affinity maturation via somatic mutation: "Heavy chain only antibodies, including their VHH or VH functional fragments, can also be produced by recombinant DNA technology, by expression

[45] WO '180 at p. 11, ln. 36 - p. 12, ln 2.
[46] *Id*.
[47] WO '180 at p. 5, lns. 24-25.
[48] *Id*. at p. 11, lns. 20-24.

of the encoding nucleic acid in a suitable eukaryotic or prokaryotic host, including E. coli or yeast."[49] This cloning process happens after affinity maturation via somatic mutation: "[T]he invention concerns a recombinant heavy chain-only immunoglobulin (Ig) locus comprising one or more human V gene segments, one or more human D gene segments, and one or more human J gene segments, which when recombined with each other in the genome of a non-human animal, and following affinity maturation, encode a heavy chain variable (VH) region."[50]

(g) After the cloning step, the UniRat® discovery platform produces a soluble, antigen-specific heavy chain only antibody. For example, "[h]eavy chain only antibodies, including their VHH or VH functional fragments, can also be produced by recombinant DNA technology, by expression of the encoding nucleic acid in a suitable eukaryotic or prokaryotic host, including E. coli or yeast."[51] Antibodies can be harvested from the discovery platform after several days of expression.[52]

86. Further and in the alternative, Defendant has been actively inducing infringement of at least claim 1 of the '970 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Methods and Products directly infringed at least claim 1 of the '970 Patent when they use the Accused Methods and Products in the ordinary, customary, and intended way as set forth in Teneobio's publications, which include but are not limited to those cited above. Defendant's inducements included, without limitation and with specific intent to encourage the infringement, knowingly inducing consumers to use the Accused Methods and Products within the United States in the ordinary, customary, and intended way by, directly or through intermediaries, supplying the Accused Methods and Products to consumers within the United States and instructing and

[49] *Id*. at p. 14, lns. 7-10.
[50] *Id*. at p. 5, lns. 16-19.
[51] WO '180 at p. 14, lns. 7-10.
[52] *Clarke, et al.*, at 10.

encouraging such customers (for example, by offering the UniRat® discovery platform) how to use the Accused Methods and Products in the ordinary, customary, and intended way, which Defendant knows or should know infringes at least claim 1 of the ’970 Patent.

87. Defendant’s inducements may further include, without limitation and with specific intent to encourage the infringement, knowingly inducing customers to use the Accused Methods and Products within the United States, or knowingly inducing customers to use the Accused Methods and Products within the United States, by, directly or through intermediaries, instructing and encouraging such customers to make, use, sell, or offer to sell the Accused Methods and Products in the United States, which Defendant knows or should know infringes at least claim 1 of the ’970 Patent.

88. Further and in the alternative, Defendant has been actively contributing to infringement of at least claim 1 of the ’970 Patent in violation of 35 U.S.C. § 271(c). Defendant has offered for sale the UniRat®, which is especially made or especially adapted to practice the invention claimed in at least claim 1 of the ’970 Patent. The UniRat® constitutes a material part of the claimed invention recited in at least claim 1 of the ’970 Patent and is not a staple article or commodity of commerce because it is specifically configured according to at least claim 1 of the ’970 Patent. Defendant’s contributions include, without limitation, making, offering to sell, and/or selling within the United States, and/or importing into the United States, the Accused Methods and Products, which includes one or more components for use in practicing the patented process, knowing the component to be especially made or especially adapted for use in an infringement of at least claim 1 of the ’970 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

89. By reason of the foregoing allegations, Defendant knew or should have known of the ’970 Patent since its issuance but was willfully blind to the existence of the ’970 Patent. Defendant has had actual knowledge of Plaintiffs on-going prosecution of the application that led to the’420 Patent since at least October 6, 2017. *See supra*, Factual Background, § D. By the time this matter is adjudicated, Defendant will have known or should have known about the ’970 Patent for several years and nevertheless intended that its actions during that time would infringe and actively induce and contribute to the infringement of one or more claims of the ’970 Patent. Defendant’s infringement of the ’970 Patent has been willful and deliberate.

90. Defendant’s infringement has caused past and will cause ongoing injury to Plaintiffs. Plaintiffs are entitled to recover damages adequate to compensate for Defendant’s infringement. Because Defendant’s infringement has been and continues to be willful and deliberate, the Court should award enhanced damages under 35 U.S.C. § 284 and find this case exceptional and award attorney’s fees under 35 U.S.C. § 285.

91. Plaintiffs have suffered and will continue to suffer irreparable injury as a direct and proximate result of Defendant’s infringement for which there is no adequate remedy at law. Unless Defendant is enjoined, Plaintiffs will continue to suffer such irreparable injury.

92. Defendant’s infringement has been without authority and/or license from Plaintiffs.

COUNT IV
INFRINGEMENT OF THE U.S. PATENT NO. 10,993,420

93. The allegations of each foregoing paragraph are incorporated by reference as if fully set forth herein and from the basis for the following cause of action against Defendant.

94. The Accused Methods and Products are covered by at least claim 1 of the ’420 Patent.

95. Claim 1 of the ’420 Patent recites:

> A method for the production of a VH heavy chain-only antibody in a transgenic non-human mammal comprising the steps of
> (a) expressing a transgene comprising a heterologous VH heavy chain locus in said mammal, wherein said locus comprises human VH gene segments and is incorporated into the genome of said mammal, wherein the VH heavy chain locus does not comprise all subclasses of human VH gene segments, and further wherein said heavy chain locus comprises three or more human VH3 gene segments, or three or more human VH3 and one or more human VH4 gene segments, one or more D gene segments, one or more J gene segments and a constant heavy chain region which does not encode a CH1 domain, and
> (b) isolating VH heavy chain-only antibody,
> wherein said VH3 gene segments comprise at least one of VH3-66 or VH3-9, said mammal is a rat or mouse, and the endogenous heavy chain locus and one or both of the endogenous light chain loci of said rat or mouse has been silenced.

96. Defendant has infringed and continues to infringe, directly and/or under the doctrine of equivalents, at least claim 1 of the ’420 Patent in violation of 35 U.S.C. § 271(a) by, directly or through intermediaries and without HBAB’s authority, making, using, selling, and/or offering to sell the Accused Methods and Products in the United States.

97. By way of illustration and not as a limitation to the full scope of its infringing activities, Teneobio infringes claim 1 of the ’420 Patent by having designed and used the UniRat® discovery platform to produce antigen-specific heavy chain only antibodies as follows:

(a) The UniRat® discovery platform produces a VH heavy chain-only antibody in a transgenic non-human mammal. For example, Teneobio’s UniRat® discovery platform is a method “[f]or the generation of antigen-specific heavy chain-only antibodies in rats” by immunizing “genetically engineered rats expressing heavy chain only antibodies.”[53]

(b) Teneobio expresses a transgene including a heterologous VH heavy chain locus in the transgenic rat. For example, the UniRats “produce chimeric HCAbs with fully human

[53] WO ’180 at p. 23, lns. 2-3; *see also Clarke, et al.*, at p. 2 (“We have created an antibody discovery platform… in transgenic rats, called UniRats, that produce heavy chain only antibodies with fully human variable domains, termed UniAbs™.”).

VH domains in response to an antigen challenge."[54] These UniRat strains are "generated, (termed HC27 and HC31), expressing different parts of a complete functional human V gene repertoire together with the full suite of human D and JH genes (Figures 1A, B)."[55] The "recombinant heavy chain-only Ig locus encodes a human or humanized heavy chain-only antibody comprising a VH region . . . In another aspect, the invention concerns a transgenic non-human animal comprising a recombinant heavy chain-only Ig locus."[56]

(c) The VH heavy chain locus is made up of human VH gene segments and is incorporated into the genome of the rat. For example, UniRats "express UniAbs due to genomic insertion of large transgenic loci accommodating the full repertoire of functional human VH, D, and JH genes . . ."[57] Furthermore, the heavy chain-only Ig locus of the UniRat discovery platform consists of "one or more human V gene segments, one or more human D segments, and one or more human J segments, which when recombined with each other in the genome of a non-human animal, and following affinity maturation, encode a heavy chain variable (VH) region."[58]

(d) The VH heavy chain locus of the UniRat discovery platform does not comprise all subclasses of human VH gene segments. For example, the UniRat strains are "generated, (termed HC27 and HC31), expressing different parts of a complete functional human V gene repertoire together with the full suite of human D and JH genes (Figures 1A,B)."[59]

(e) The heavy chain locus of the Teneobio's discovery platform includes three or more human VH3 gene segments, or three or more human VH3 and one or more human VH4

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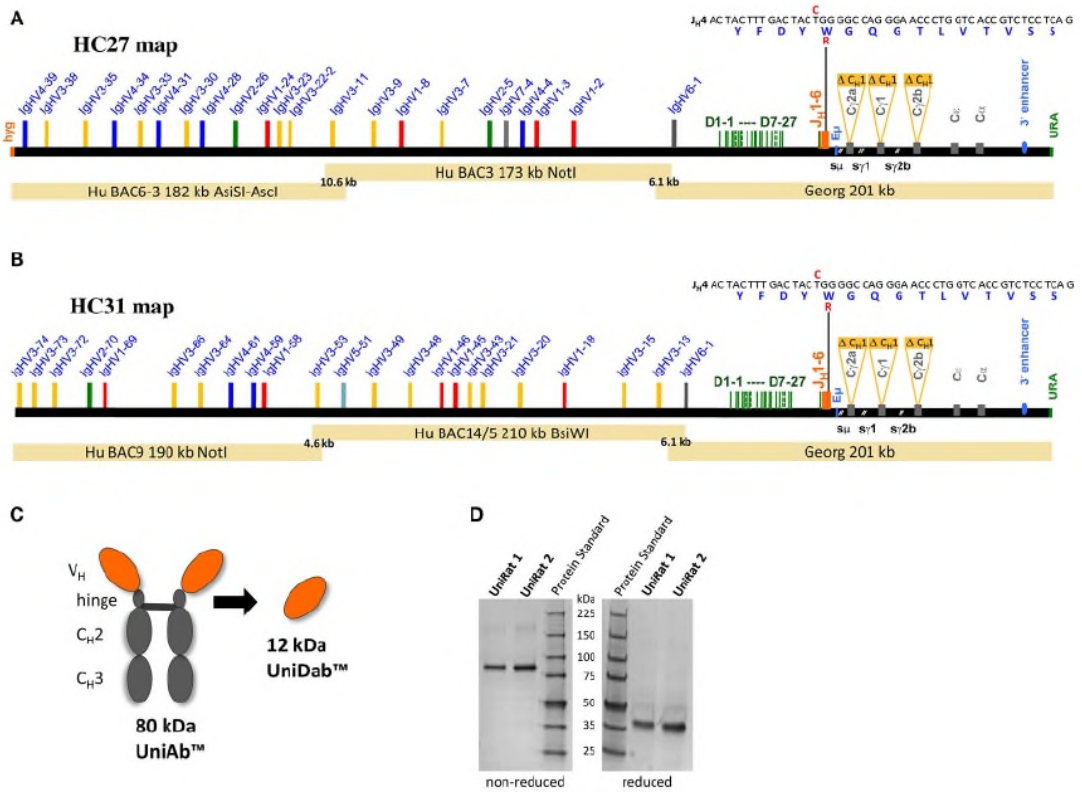
[54] *Clarke, et al.*, at Abstract.
[55] *Id.* at 2.
[56] WO '180 at p. 6, lns. 7-10.
[57] *Clarke, et al.*, at 2.
[58] WO '180 at Claim 32.
[59] *Clarke, et al.*, at 2 (Figs 1A and 1B show the respective parts of the human V genome in each strain).

gene segments, one or more D gene segments, one or more J gene segments and a constant heavy chain region which does not encode a CH1 domain. For example, Figure 1 (reproduced below), shows "two UniRat strains expressing different sets of human V genes, HC27 (A) and HC31 (B)," each having three or more human VH3 gene segments, one or more human VH4 gene segments, one or more D gene segments, one or more J gene segments, and deleted CH1 segments. Moreover, "[c]onstruction of UniRat Strains . . . [l] arge IgH loci on BACs carrying human VH, D and JH segments in germline configuration linked to rat Cγ genes were compiled as detailed previously . . . except that a new assembly of rat CH genes lacking CH1 domains was used."[60] To enable heavy chain antibody expression, Teneobio reassembles a rat constant region BAC "by replacement of Cμ and adjacent 3' regions with Cγ2α as the first gene followed by Cγ1 and Cγ2b; all with CH1 exons removed."[61]

[60] *Clarke, et al.*, at p. 2.
[61] *Id.* at 9, Fig. 1A.



(f) Teneobio isolates the VH heavy chain-only antibody. For example, antibodies from Teneobio's discovery platform can be harvested from the discovery platform after several days of expression.[62]

(g) Teneobio's VH3 gene segments include at least one of VH3-66 or VH3-9. For example, as depicted above in Figures 1A and 1B of *Clarke, et al.*, UniRat strain HC27 expresses VH3-9, and UniRat strain HC31 expresses VH3-66.

(h) The UniRat "BAC6 contains the human genomic region from VH4-39 to VH3-23, while BAC3 contains a downstream region from VH3-1 1 to VH6-1 (the most D proximal VH gene)... Both fragments were purified and co-injected with the ~ 201 kb Notl fragment from Georg II into rat embryos to construct HC32."[63]

[62] *Id*. at 10.
[63] WO '180 p. 20, lns. 29-35.

(i) Furthermore, the UniRat "BAC9 contains the human genomic region from VH3-74 to VH3-53. BAC(14+5) contains a downstream region from VH3-53 to VH3-13 and a 6.1 kb region immediately upstream of VH6-1 was added to its 3' to provide an overlap to Georg II . . . Both fragments were purified and co-injected with the ~ 201 kb NotI fragment from Georg II into rat embryos to construct HC33."[64]

(j) The mammal used by Teneobio is a rat. For example, the Teneobio discovery platform uses "transgenic rats, called UniRats."[65]

(k) The endogenous heavy chain locus and one or both of the endogenous light chain loci of said rat has been silenced. For example, the "UniRats express UniAbs . . . while endogenous rat Ig expression has been silenced by targeted disruption of the IgH, Igκ and Igλ loci with inserted zinc-finger-nuclease constructs."[66] The heavy chain-only expression in the UniRats is "enforced by silencing of the endogenous heavy and light chain (kappa and lambda) loci."[67]

98. Further and in the alternative, Defendant has been actively inducing infringement of at least claim 1 of the '420 Patent in violation of 35 U.S.C. § 271(b). Users of the Accused Methods and Products directly infringed at least claim 1 of the '420 Patent when they use the Accused Methods and Products in the ordinary, customary, and intended way. Defendant's inducements included, without limitation and with specific intent to encourage the infringement, knowingly inducing consumers to use the Accused Methods and Products within the United States in the ordinary, customary, and intended way by, directly or through intermediaries, supplying the Accused Methods and Products to consumers within the United States and instructing and encouraging such customers (for example, by offering the UniRat® discovery platform) how to

[64] *Id.* at p. 20, ln. 36 – p. 21, ln. 3.
[65] *Clarke, et al.*, at Abstract.
[66] *Id.* at p. 2.
[67] WO '180 at p. 16, lns. 24-26.

use the Accused Methods and Products in the ordinary, customary, and intended way, which Defendant knows or should know infringes at least claim 1 of the ’420 Patent.

99. Defendant’s inducements may further include, without limitation and with specific intent to encourage the infringement, knowingly inducing customers to use the Accused Methods and Products within the United States, or knowingly inducing customers to use the Accused Methods and Products within the United States, by, directly or through intermediaries, instructing and encouraging such customers to make, use, sell, or offer to sell the Accused Methods and Products in the United States, which Defendant knows or should know infringes at least claim1 of the ’420 Patent.

100. Further and in the alternative, Defendant has been actively contributing to infringement of at least claim 1 of the ’420 Patent in violation of 35 U.S.C. § 271(c). Defendant has offered for sale the UniRat®, which is especially made or especially adapted to practice the invention claimed in at least claim 1 of the ’420 Patent. The UniRat® constitutes a material part of the claimed invention recited in at least claim 1 of the ’420 Patent and is not a staple article or commodity of commerce because it is specifically configured according to at least claim 1 of the ’420 Patent. Defendant’s contributions include, without limitation, making, offering to sell, and/or selling within the United States, and/or importing into the United States, the Accused Methods and Products, which include one or more components for use in practicing the patented process, knowing the component to be especially made or especially adapted for use in an infringement of at least claim 1 of the ’420 Patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use.

101. By reason of the foregoing allegations, Defendant knew or should have known of the ’420 Patent since its issuance but was willfully blind to the existence of the ’420 Patent.

Defendant has had actual knowledge of Plaintiffs on-going prosecution of the application that led to the'420 Patent since at least October 6, 2017. *See supra*, Factual Background, § D. By the time this matter is adjudicated, Defendant will have known or should have known about the '420 Patent for many years and nevertheless intended that its actions during that time would infringe and actively induce and contribute to the infringement of one or more claims of the '420 Patent. Defendant's infringement of the '420 Patent has been willful and deliberate.

102. Defendant's infringement has caused past and will cause ongoing injury to Plaintiffs. Plaintiffs are entitled to recover damages adequate to compensate for Defendant's infringement. Because Defendant's infringement has been and continues to be willful and deliberate, the Court should award enhanced damages under 35 U.S.C. § 284 and find this case exceptional and award attorney's fees under 35 U.S.C. § 285.

103. Plaintiffs have suffered and will continue to suffer irreparable injury as a direct and proximate result of Defendant's infringement for which there is no adequate remedy at law. Unless Defendant is enjoined, Plaintiffs will continue to suffer such irreparable injury.

104. Defendant's infringement has been without authority and/or license from Plaintiffs.

DEMAND FOR JURY TRIAL

105. Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs request a jury trial of all issues triable of right by a jury.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court enter an order providing the following relief:

(a) A judgment in favor of Plaintiffs that Defendant has infringed each Asserted Patent, whether literally or under the doctrine of equivalents;

(b) A judgment that such infringement of each Asserted Patent has been willful and deliberate as described herein;

(c) A judgment and order permanently enjoining Defendant, its officers, agents, servants, employees, attorneys, and all those persons in active concert or participation with it, from further acts of infringement of the Asserted Patents pursuant to 35 U.S.C. § 283;

(d) A judgment and order requiring Defendant to pay Plaintiffs their damages, costs, expenses, and pre-judgment and post-judgment interest for Defendant's infringement of each Asserted Patent as provided under 35 U.S.C. § 284, including supplemental damages for any continuing post-verdict or post-judgment infringement with an accounting as needed;

(e) A judgment and order requiring Defendant to pay Plaintiffs enhanced damages for willful infringement as provided under 35 U.S.C. § 284;

(f) A judgment and order finding this case exceptional and requiring Defendant to pay Plaintiffs its reasonable attorneys' fees and costs incurred in this litigation pursuant to 35 U.S.C. § 285, together with pre-judgment and post-judgment interest thereon; and

(g) Awarding Plaintiffs all such other and further relief, in law or equity, as the Court deems just and proper under the circumstances.

Dated: December 23, 2021

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