IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ACERTA PHARMA B.V., ASTRAZENECA UK LTD., and ASTRAZENECA PHARMACEUTICALS LP, Plaintiffs, v. PHARMACYCLICS LLC, and ABBVIE, INC., Defendants.	Civil Action No. _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Acerta Pharma B.V., AstraZeneca UK Ltd., and AstraZeneca Pharmaceuticals LP, by their attorneys, bring this Complaint against Defendants Pharmacyclics LLC and AbbVie Inc. pursuant to 35 U.S.C. § 271, § 284, and § 285 for damages and other relief as a remedy for Defendants' infringement of U.S. Patent No. 7,459,554 through the manufacture, offer to sell, sale, and importation of Imbruvica® and ibrutinib.

NATURE OF THE CASE

1. This is an action for patent infringement under the patent laws of the United States, Title 35, United States Code, that arises out of Defendants' manufacture, offers to sell, sale, and importation of their Bruton tyrosine kinase inhibitor drug Imbruvica®. Plaintiffs own, exclusively license, and practice patents relating to compounds that inhibit tyrosine kinases, including the '554 patent. The active ingredient in Imbruvica®, ibrutinib, falls within the equivalent scope of certain claims of the '554 patent, and Defendants thus infringe the '554 patent by manufacturing, offering to sell, selling, and importing Imbruvica® and its active

ingredient, ibrutinib. Defendants also induce and contribute to the infringement of the '554 patent by physicians that prescribe and patients that receive Imbruvica®.

PARTIES, JURISDICTION, AND VENUE

2. Plaintiff Acerta Pharma B.V. is a private limited liability company organized and existing under the laws of the Netherlands, having its principal place of business at Kloosterstraat 9, 5349 AB Oss, The Netherlands.

3. Plaintiff AstraZeneca UK Ltd. is a private company limited by shares organized and existing under the laws of England and Wales, having its principal place of business at 1 Francis Crick Avenue, Cambridge Biomedical Campus, Cambridge CB2 0AA, United Kingdom.

4. Plaintiff AstraZeneca Pharmaceuticals LP is a limited partnership organized and existing under the laws of Delaware, having its principal place of business at 1800 Concord Pike, P.O. Box 15437, Wilmington, Delaware 19850.

5. On information and belief, Defendant Pharmacyclics LLC is a limited liability company organized and existing under the laws of Delaware, having its principal place of business at 999 East Arques Avenue, Sunnyvale, California 94085.

6. On information and belief, Defendant AbbVie Inc. is a corporation organized and existing under the laws of Delaware, having its principal place of business at 1 North Waukegan Road, North Chicago, Illinois 60064-6400.

7. This Court has personal jurisdiction over AbbVie Inc. and Pharmacyclics LLC because, among other things, they regularly transact and/or solicit business in Delaware and have purposefully availed themselves of this forum such that they should reasonably anticipate being hailed into court here.

8. This Court has personal jurisdiction over AbbVie Inc. because AbbVie Inc. is a corporation organized and existing under the laws of Delaware

9. This Court has personal jurisdiction over Pharmacyclics LLC because Pharmacyclics LLC is a limited liability company organized and existing under the laws of Delaware.

10. Venue is proper as to AbbVie Inc. and Pharmacyclics LLC in the District of Delaware because AbbVie Inc. and Pharmacyclics LLC have committed acts of infringement and have a regular place of business in the District of Delaware.

11. Venue is proper as to AbbVie Inc. because AbbVie Inc. is a corporation organized and existing under the laws of Delaware.

12. Venue is proper as to Pharmacyclics LLC because Pharmacyclics LLC is a Delaware limited liability company organized and existing under the laws of Delaware.

BACKGROUND

13. Plaintiffs are world leaders in researching, developing, and bringing to market revolutionary pharmaceutical products to help patients prevail against serious diseases, including treatments for hematologic cancers.

14. Plaintiffs discovered and developed Calquence®, a novel oncology therapy indicated for the treatment of adult patients with mantle cell lymphoma, an aggressive type of blood cancer, who have received at least one prior therapy. Mantle cell lymphoma is a fast-growing type of non-Hodgkin lymphoma that often has spread to the lymph nodes, bone marrow, and other organs at the time of diagnosis.

15. The U.S. Food and Drug Administration granted Calquence® accelerated approval on October 31, 2017 for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy. FDA's Accelerated Approval Program was established to "allow for earlier approval of drugs that treat serious conditions, and that fill an unmet medical

need based on a surrogate endpoint."[1] Calquence®'s approval followed a Phase II clinical trial in which 80% of patients receiving Calquence® achieved an overall response and 40% of patients achieved a complete response.

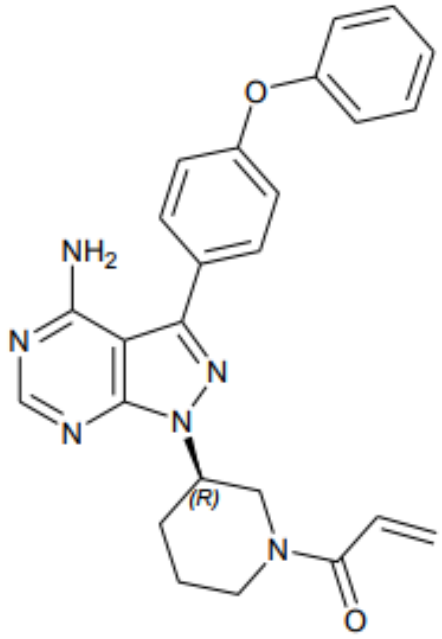
16. The active ingredient in Calquence® is acalabrutinib, a highly selective inhibitor of Bruton tyrosine kinase ("BTK").

17. AbbVie Inc. and Pharmacyclics LLC market a drug product containing a different, less selective, BTK inhibitor for the treatment of cancer, including for the treatment of patients with mantle cell lymphoma who have received at least one prior therapy, under the trade name Imbruvica®.

18. Imbruvica® first received accelerated approval from the FDA in 2013 for the treatment of patients with mantle cell lymphoma who have received at least on prior therapy. Imbruvica® subsequently received FDA approval for the treatment of patients with, among other diseases, chronic lymphocytic leukemia and small lymphocytic lymphoma.

[1] FDA, *Accelerated Approval Program*, https://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals/ucm313768.htm. Accelerated approval is conditional upon verification and description of clinical benefit in confirmatory trials.

19. The active ingredient in Imbruvica® is 1-[(3*R*)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one, also known as ibrutinib, which has the following structure:



20. On information and belief, the ibrutinib active pharmaceutical ingredient in Imbruvica® is manufactured in China.

21. On information and belief, the ibrutinib active pharmaceutical ingredient in Imbruvica® is imported into the United States at the direction and under the control of Defendants.

22. On information and belief, Pharmacyclics LLC has been manufacturing, offering to sell, selling, and/or importing Imbruvica® and/or ibrutinib in the United States since 2013, and continues to do so to this day.

23. On information and belief, Pharmacyclics LLC markets and sells Imbruvica® and/or ibrutinib as the agent of AbbVie Inc.

THE ’554 PATENT

24. On December 2, 2008, the United States Patent and Trademark Office issued U.S. Patent No. 7,459,554, entitled “Imidazopyrazine Tyrosine Kinase Inhibitors” (Ex. A). The ’554 patent claims a novel class of molecules, which act as inhibitors of tyrosine kinases, including BTK.

25. OSI Pharmaceuticals Inc. was the assignee of the ’554 patent at the time it was issued.

26. On March 31, 2011, OSI Pharmaceuticals Inc. was converted into OSI Pharmaceuticals LLC, and all right, title, and interest in and to the ’554 patent transferred from OSI Pharmaceuticals Inc. to OSI Pharmaceuticals LLC.

27. In 2013, OSI Pharmaceuticals LLC transferred all right, title, and interest in and to, *inter alia*, the ’554 patent to Acerta Pharma B.V.

28. AstraZeneca UK Ltd. is the exclusive licensee of the ’554 patent from Acerta Pharma B.V. and has the right to sublicense any or all of its rights to third parties. AstraZeneca Pharmaceuticals LP is the exclusive distributor and seller of Calquence® in the United States.

29. AstraZeneca UK Ltd. holds NDA No. 210259 for Calquence®, and, pursuant to 21 U.S.C. § 355(b)(3)(C) and 355(j)(2)(B)(iii), and 21 C.F.R. §§ 314.52(a)(2) and 314.95(a)(1), AstraZeneca Pharmaceuticals LP is designated as the U.S. agent for NDA No. 210259 for Calquence®.

30. The ’554 patent is listed in the FDA’s Approved Drug Products with Therapeutic Equivalence Evaluations (“Orange Book”) for Calquence®.

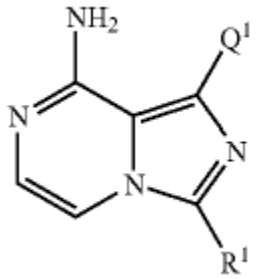
COUNT I
(Infringement of U.S. Patent No. 7,459,554)

31. On information and belief, during the term of the ’554 patent, Defendants have

manufactured, offered to sell, sold, and/or imported Imbruvica® and ibrutinib.

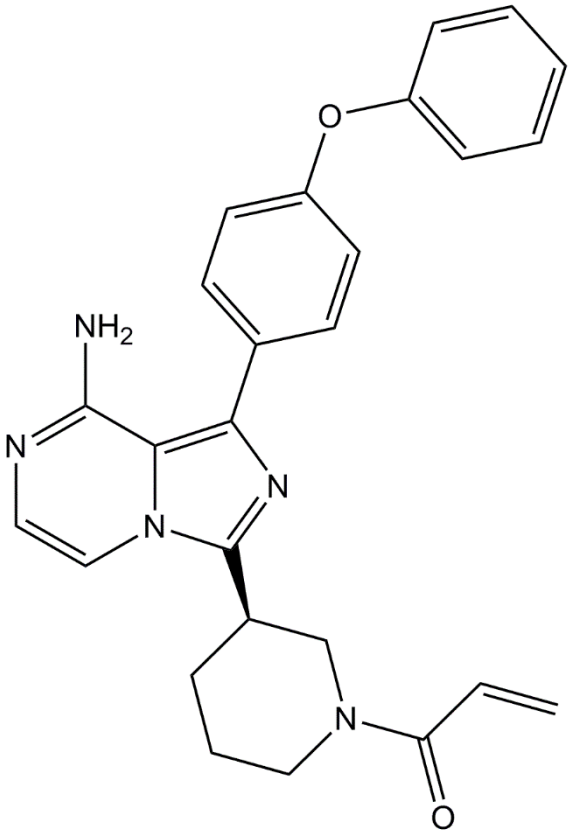
32. Defendants' manufacture, offers to sell, and sale of Imbruvica® (ibrutinib) within the United States, and/or importation of Imbruvica® (ibrutinib) into the United States, during the term of the '554 patent, infringes claim 16 of the '554 patent under the doctrine of equivalents.

33. Specifically, claim 16 of the '554 patent recites a compound represented by Formula I:

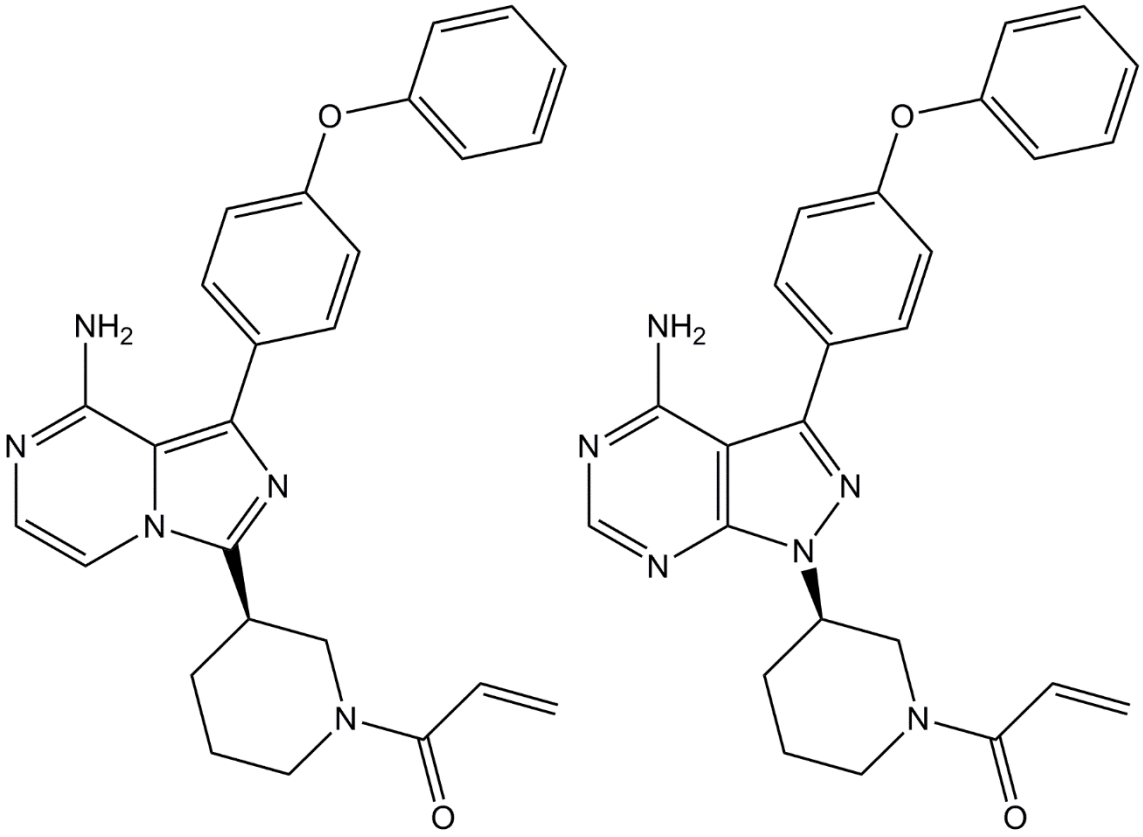


Claim 16 further permits Q^1 to be $aryl^1$ substituted by G^1, wherein G^1 is $–OR^2$, R^2 is aryl-C_{0-10}alkyl, aryl is phenyl, and C_{0-10}alkyl is C_0alkyl. Claim 16 further requires R^1 to be heterocyclyl and permits substitution by G^{11}, wherein G^{11} is $–C(O)R^{21}$, R^{21} is C_{2-10}alkenyl, and C_{2-10}alkenyl is $–CH=CH_2$.

34. 1-[(3*R*)-3-[8-amino-1-(4-phenoxyphenyl)-imidazo[1,5-a]pyrazin-3-yl]-1-piperidinyl]-2-propen-1-one, depicted below, is within the scope of claim 16.



35. 1-[(3*R*)-3-[8-amino-1-(4-phenoxyphenyl)-imidazo[1,5-a]pyrazin-3-yl]-1-piperidinyl]-2-propen-1-one and 1-[(3*R*)-3-[4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl]-1-piperidinyl]-2-propen-1-one (ibrutinib) are identical in structure except for their respective imidazo[1,5-a]pyrazine and pyrazolo[3,4-d]pyrimidine cores, as shown below.



36. With respect to the compounds recited and depicted in paragraphs 34 and 35, the imidazo[1,5-a]pyrazine core and the pyrazolo[3,4-d]pyrimidine core both function to facilitate binding to and inhibition of a tyrosine kinase.

37. With respect to the compounds recited and depicted in paragraphs 34 and 35, the pyrazolo[3,4-d]pyrimidine core is insubstantially different from the imidazo[1,5-a]pyrazine core.

38. The pyrazolo[3,4-d]pyrimidine core in ibrutinib and imidazo[1,5-a]pyrazine core in 1-[(3*R*)-3-[8-amino-1-(4-phenoxyphenyl)-imidazo[1,5-a]pyrazin-3-yl]-1-piperidinyl]-2-propen-1-one perform substantially the same function, in substantially the same way, to achieve substantially the same result.

39. Accordingly, Imbruvica® and ibrutinib infringe claim 16 of the ’554 patent under the doctrine of equivalents.

40. The manufacture, offer to sell, sale, and/or importation of Imbruvica® and/or

ibrutinib by Pharmacyclics LLC directly infringes claim 16 of the ’554 patent under 35 U.S.C. § 271(a).

41. On information and belief, Imbruvica® and ibrutinib are not staple articles or commodities of commerce suitable for substantial noninfringing use and have no substantial noninfringing uses.

42. On information and belief, Pharmacyclics LLC has knowledge of the ’554 patent, at least as of November 3, 2017.

43. On information and belief, AbbVie Inc. has knowledge of the ’554 patent, at least as of November 3, 2017.

44. On information and belief, this infringing manufacture, offer to sell, sale, or importation of Imbruvica® and ibrutinib by Pharmacyclics LLC is at AbbVie Inc.’s behest, and with its intent, knowledge, and encouragement, and AbbVie Inc. will actively induce, encourage, contribute to, aid, and abet this manufacture, offer to sell, sale, or importation with knowledge that it is in contravention of the ’554 patent.

45. As a result, AbbVie Inc. is liable under 35 U.S.C. §§ 271(b) and/or (c) for inducing and/or contributing to infringement of the ’554 patent by Pharmacyclics LLC.

46. The use of Imbruvica® (ibrutinib) by physicians and patients directly infringes claim 16 of the ’554 patent under 35 U.S.C. § 271(a).

47. On information and belief, this infringing use of Imbruvica® (ibrutinib) by physicians and patients is at Defendants’ behest, and with their intent, knowledge, and encouragement, and Defendants will actively induce, encourage, contribute to, aid, and abet this use with knowledge that it is in contravention of the ’554 patent.

48. As a result, Defendants are liable under 35 U.S.C. §§ 271(b) and/or (c) for

inducing and/or contributing to infringement of the ’554 patent by physicians and patients who use Imbruvica® (ibrutinib).

49. Plaintiffs have been damaged by Defendants’ infringement of the ’554 patent. Plaintiffs have a right to recover from Defendants the damages sustained by Plaintiffs as a result of Defendants’ wrongful acts.

50. Defendants’ infringement of the ’554 patent has been with full and complete knowledge of the ’554 patent and its applicability to Imbruvica® and ibrutinib without a good faith belief that the ’554 patent is invalid or not infringed.

51. Defendants’ infringement has been deliberate and willful, which permits Plaintiffs to seek enhanced damages under 35 U.S.C. § 284 and attorneys’ fees and costs incurred in prosecuting this action under 35 U.S.C. § 285.

JURY DEMAND

52. Plaintiffs request a trial by jury on all issues so triable.

* * *

WHEREFORE, Plaintiffs therefore respectfully request the following relief:

1. A judgment that the ’554 patent is infringed by Pharmacyclics LLC’s manufacture, offers to sell, sales, and uses within the United States, and importation into the United States, of Imbruvica® and/or ibrutinib;

2. A judgment that Pharmacyclics LLC’s manufacture, offers to sell, sales, and uses within the United States, and importation into the United States, of Imbruvica® and/or ibrutinib has induced and contributed to the infringement of the ’554 patent by others;

3. A judgment that AbbVie Inc. has induced and contributed to the infringement of the ’554 patent;

4. Actual damages, including a reasonable royalty and lost profits, together with

prejudgment interest;

5. That Defendants' infringement be deemed willful and that Plaintiffs be awarded enhanced damages under 35 U.S.C. § 284;

6. A declaration that this is an exceptional case and an award of Plaintiffs' attorneys' fees pursuant to 35 U.S.C. § 285;

7. An award to Plaintiffs of their costs and expenses in this action; and

8. Such further and additional relief as this Court deems just and proper.

Dated: April 18, 2018

MORGAN, LEWIS & BOCKIUS LLP

/s/ David W. Marston Jr.

David W. Marston Jr. (No. 3972)
Jody C. Barillare (No. 5107)
Amy M. Dudash (No. 5741)
The Nemours Building
1007 North Orange Street
Suite 501
Wilmington, DE 19801
(302) 574-3000
david.marston@morganlewis.com
jody.barillare@morganlewis.com
amy.dudash@morganlewis.com

OF COUNSEL:

Eric Kraeutler
John V. Gorman
MORGAN, LEWIS & BOCKIUS LLP
1701 Market Street
Philadelphia, PA 19103-2921
(215) 963-5000
eric.kraeutler@morganlewis.com
john.gorman@morganlewis.com

Olga Berson, Ph.D.
2049 Century Park East

YOUNG CONAWAY STARGATT & TAYLOR, LLP

/s/ Adam W. Poff

Adam W. Poff (No. 3990)
Pilar G. Kraman (No. 5199)
Rodney Square
1000 North King Street
Wilmington, DE 19801
(302) 571-6600
apoff@ycst.com
pkraman@ycst.com

OF COUNSEL:

David I. Berl
Dov P. Grossman
Stanley E. Fisher
Galina I. Fomenkova
Teagan J. Gregory (No. 5852)
Kevin Hoagland-Hanson
WILLIAMS & CONNOLLY LLP
Twelfth Street, NW
Washington, DC 20005
(202) 434-5000
dberl@wc.com
dgrossman@wc.com
sfisher@wc.com
gfomenkova@wc.com

Suite 700
Los Angeles, CA 90067-3109
(310) 907-1000
olga.berson@morganlewis.com

Attorneys for Plaintiff Acerta Pharma B.V.

tgregory@wc.com
khoagland-hanson@wc.com

Attorneys for Plaintiffs AstraZeneca UK Ltd. and AstraZeneca Pharmaceuticals LP