IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

H. LUNDBECK A/S, TAKEDA PHARMACEUTICAL COMPANY LTD., TAKEDA PHARMACEUTICALS U.S.A., INC., TAKEDA PHARMACEUTICALS INTERNATIONAL AG, and TAKEDA PHARMACEUTICALS AMERICA, INC.,	)
Plaintiffs,	)
v.	) C.A. No. 18-150-LPS
ZYDUS PHARMACEUTICALS (USA) INC. and CADILA HEALTHCARE LTD.,	)
Defendants.	)

DEFENDANTS' ANSWER AND AFFIRMATIVE DEFENSES
TO PLAINTIFFS' FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Zydus Pharmaceuticals (USA) Inc. ("Zydus") and Cadila Healthcare Limited ("Cadila") (collectively, "Defendants") for their Answer and Affirmative Defenses to the First Amended Complaint of H. Lundbeck A/S ("Lundbeck"), Takeda Pharmaceutical Company Ltd., Takeda Pharmaceuticals U.S.A., Inc. ("Takeda USA"), Takeda Pharmaceuticals International AG, and Takeda Pharmaceuticals America, Inc. (collectively, "Plaintiffs") state as follows:

All averments not expressly admitted are denied.

NATURE OF THE ACTION

1. The allegations in paragraph 1 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Plaintiffs' Complaint purports to be a civil action alleging infringement of United States Patent Nos. 7,144,884 ("the '884 patent"), 8,476,279 ("the '279 patent"), 8,722,684 ("the '684 patent"), 8,969,355 ("the '355

patent"), 9,227,946 ("the '946 patent"), and 9,861,630 ("the '630 patent") pursuant to Title 35 of the United States Code. Defendants admit that Zydus submitted Abbreviated New Drug Application ("ANDA") No. 211146 to the United States Food and Drug Administration ("FDA") under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 identifies TRINTELLIX® (vortioxetine) tablets, 5 mg, 10 mg, and 20 mg, as the Reference Listed Drug. Defendants deny all other allegations in paragraph 1.

THE PARTIES

2. Defendants admit that according to the patent assignment listings of the United States Patent and Trademark Office (the "USPTO") at Reel No. 014825, Frame No. 0101, Reel No. 029041, Frame No. 0013, Reel No. 023137, Frame No. 0063, and Reel No. 043528, Frame No. 0434, H. Lundbeck A/S is the assignee listed for the '884, '279, '684, '355, '946, and '630 patents. Defendants lack knowledge or information sufficient to form a belief about the truth of all other allegations in paragraph 2 and therefore deny them.

3. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 3 and therefore deny them.

4. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 4 and therefore deny them.

5. Defendants admit that FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book"), lists "TAKEDA PHARMACEUTICALS USA INC" as the Applicant Holder for New Drug Application ("NDA") No. 204447, TRINTELLIX® (vortioxetine) tablets, 5 mg, 10 mg, and 20 mg. Defendants lack knowledge or information

sufficient to form a belief about the truth of all other allegations in paragraph 5 and therefore deny them.

6. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 6 and therefore deny them.

7. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 7 and therefore deny them.

8. Admitted.

9. Admitted.

10. Admitted.

11. The allegations in paragraph 11 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny the allegations in paragraph 11.

12. The allegations in paragraph 12 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Cadila manufactures pharmaceutical products, including generic pharmaceutical products. Defendants further admit that Zydus files ANDAs seeking FDA approval to market pharmaceutical products in the United States, including products manufactured by Cadila, and that Zydus sells pharmaceutical products, including products manufactured by Cadila. Defendants deny all other allegations in paragraph 12.

13. The allegations in paragraph 13 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny the allegations in paragraph 13.

14. Defendants admit that Zydus submitted ANDA No. 211146 to FDA and that Cadila assisted in the preparation of ANDA No. 211146. Defendants deny all other allegations in paragraph 14.

15. Defendants admit that Zydus submitted ANDA No. 211146 to FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg, and that Cadila assisted in the preparation of ANDA No. 211146. Defendants deny all other allegations in paragraph 15.

16. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146 and that Cadila is the manufacturer of the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 16.

17. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146 and that Cadila is the manufacturer of the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 17.

JURISDICTION AND VENUE

18. The allegations in paragraph 18 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Plaintiffs' Complaint purports to be a civil action alleging infringement of the '884, '279, '684, '355, '946, and '630 patents pursuant to Title 35 of the United States Code. Defendants deny that the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146 infringe any valid and enforceable claim of the '884, '279, '684, '355, '946, and '630 patents. Defendants deny all other allegations in paragraph 18.

19. The allegations in paragraph 19 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants do not contest subject matter jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 19.

20. The allegations in paragraph 20 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 20.

21. Defendants admit that Zydus sells pharmaceutical products, including generic pharmaceutical products, in the United States, including in this judicial district. Defendants further admit that Cadila manufactures pharmaceutical products, including generic pharmaceutical products. Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 21.

22. Defendants admit that Zydus sells pharmaceutical products in the United States, including in this judicial district. Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 22.

23. The allegations in paragraph 23 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Zydus sent a letter dated December 14, 2017 ("First Notice Letter") and a letter dated March 12, 2018 ("Second Notice Letter") (collectively, "Notice Letters") to Lundbeck and Takeda USA pursuant to 21 U.S.C. § 355(j)(2)(B), notifying Lundbeck and Takeda USA that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 23.

24. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 24.

25. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 25.

26. The allegations in paragraph 26 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 26.

27. The allegations in paragraph 27 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that: in *Biogen International*

GmbH v. Zydus Pharmaceuticals (USA) Inc., No. 1:17-cv-00954-LPS (D. Del. Oct. 16, 2017), Zydus stated that "Zydus does not contest venue or personal jurisdiction in this Court solely for purposes of Biogen's alleged claims arising under 35 U.S.C. § 271(e)(2) against Zydus in this case and solely as those alleged claims apply to the proposed products described in [the ANDA at issue]"; in *Millennium Pharmaceuticals, Inc. v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:17-cv-00423-GMS (D. Del. May 24, 2017), Defendants asserted counterclaims and stated that "Defendants do not contest personal jurisdiction in this Court for the limited purposes of this action only" and that "Defendants do not contest venue in this Court for the limited purposes of this action only"; in *Bristol-Meyers Squibb Co. v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:17-cv-00412-LPS (D. Del. May 31, 2017), Zydus stated that "Zydus does not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Zydus in this case and solely as they apply to the proposed product described in [the ANDA at issue]" and admitted to the allegation in the Complaint stating that "Zydus, through its counsel, by e-mail dated March 28, 2017, agreed that it does not contest jurisdiction or venue in this Court in this matter"; in *Pfizer Inc. v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:17-cv-00214-LPS (D. Del. June 5, 2017), Defendants stated that "Defendants do not contest personal jurisdiction in this Court solely for the purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the proposed product described in [the ANDA at issue]"; in *Sanofi-Aventis U.S. LLC v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:17-cv-00034-GMS (D. Del. Apr. 10, 2017), Defendants asserted counterclaims and stated that "Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the proposed product described in [the ANDA at issue]" and that "Defendants do not contest venue in this judicial district solely for purposes of Plaintiffs' claims against Defendants

in this case and solely as they apply to the proposed product described in [the ANDA at issue]"; in *Astellas Pharma Inc. v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:16-cv-01167-GMS (D. Del. Feb. 27, 2017), Defendants asserted counterclaims and stated that "Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the proposed product described in [the ANDA at issue]" and that "Defendants do not contest venue in this judicial district solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the proposed product described in [the ANDA at issue]"; in *Genzyme Corp. v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:16-cv-00540-KAJ (D. Del. July 20, 2016), Zydus asserted counterclaims and stated that "Zydus does not contest personal jurisdiction in this Court solely for purposes of Genzyme's claims against Zydus in this case" and that "Zydus does not contest venue in this Court solely for purposes of Genzyme's claims against Zydus in this case"; and, in *Upsher-Smith Laboratories, Inc. v. Zydus Pharmaceuticals (USA) Inc.*, No. 1:16-cv-00248-SLR (D. Del. Oct. 31, 2016), Defendants asserted counterclaims and stated that "Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed product described in [the ANDA at issue]" and that "Defendants do not contest venue in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed product described in [the ANDA at issue]." Defendants deny all other allegations in paragraph 27.

28. The allegations in paragraph 28 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants do not contest venue in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply

to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 28.

29. The allegations in paragraph 29 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants do not contest venue in this Court solely for purposes of Plaintiffs' claims against Defendants in this case and solely as they apply to the vortioxetine tablets, 5 mg, 10 mg, and 20 mg, described in ANDA No. 211146. Defendants deny all other allegations in paragraph 29.

PLAINTIFFS' APPROVED TRINTELLIX® DRUG PRODUCT AND PATENTS

30. Defendants admit that the FDA's Orange Book lists "TAKEDA PHARMACEUTICALS USA INC" as the Applicant Holder and lists "VORTIOXETINE HYDROBROMIDE" as the Active Ingredient for NDA No. 204447, TRINTELLIX® (vortioxetine) tablets, 5 mg, 10 mg, 15 mg, and 20 mg. Defendants further admit that the FDA's Orange Book lists September 30, 2013, as the approval date for NDA No. 204447. Defendants deny all other allegations in paragraph 30.

31. Defendants admit that the prescribing information for TRINTELLIX® (Revised 4/2017) states, in part, "TRINTELLIX is indicated for the treatment of major depressive disorder (MDD) (1, 14)." Defendants further admit that the prescribing information for TRINTELLIX® (Revised 4/2017) states, in part:

> **12.1 Mechanism of Action**
> The mechanism of the antidepressant effect of vortioxetine is not fully understood, but is thought to be related to its enhancement of serotonergic activity in the CNS through inhibition of the reuptake of serotonin (5-HT). It also has several other activities including 5-HT3 receptor antagonism and 5-HT1A receptor agonism. The contribution of these activities to vortioxetine's antidepressant effect has not been established.

Defendants lack knowledge or information sufficient to form a belief about the truth of all other allegations in paragraph 31 and therefore deny them.

32. Defendants admit that the ’884, ’279, ’684, ’355, ’946, and ’630 patents are listed in the FDA’s Orange Book for NDA No. 204447, TRINTELLIX® (vortioxetine) tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 32.

33. Defendants admit on information and belief that what purports to be a copy of the ’884 patent is attached to the Complaint as Exhibit A. Defendants further admit that Exhibit A is titled “Phenyl-piperazine Derivatives as Serotonin Reuptake Inhibitors” and lists December 5, 2006 as the “Date of Patent.” Defendants deny all other allegations in paragraph 33.

34. Defendants admit on information and belief that what purports to be a copy of the ’279 patent is attached to the Complaint as Exhibit B. Defendants further admit that Exhibit B is titled “Phenyl-piperazine Derivatives as Serotonin Reuptake Inhibitors” and lists July 2, 2013 as the “Date of Patent.” Defendants deny all other allegations in paragraph 34.

35. Defendants admit on information and belief that what purports to be a copy of the ’684 patent is attached to the Complaint as Exhibit C. Defendants further admit that Exhibit C is titled “1-[2-(2,4-Dimethylphenylsulfanyl)-phenyl] Piperazine as a Compound with Combined Serotonin Reuptake, 5-HT3 and 5-HT1A Activity for the Treatment of Cognitive Impairment” and lists May 13, 2014 as the “Date of Patent.” Defendants deny all other allegations in paragraph 35.

36. Defendants admit on information and belief that what purports to be a copy of the ’355 patent is attached to the Complaint as Exhibit D. Defendants further admit that Exhibit D is titled “1-[2-(2,4-Dimethylphenylsulfanyl)-phenyl]piperazine as a Compound with Combined Serotonin Reuptake, 5-HT3 and 5-HT1A Activity for the Treatment of Cognitive Impairment” and lists March 3, 2015 as the “Date of Patent.” Defendants deny all other allegations in paragraph 36.

37. Defendants admit on information and belief that what purports to be a copy of the '946 patent is attached to the Complaint as Exhibit E. Defendants further admit that Exhibit E is titled "1-[2-(2,4-Dimethylphenylsulfanyl)-phenyl]piperazine as a Compound with Combined Serotonin Reuptake, 5-HT3 and 5-HT1A Activity for the Treatment of Cognitive Impairment" and lists January 5, 2016 as the "Date of Patent." Defendants deny all other allegations in paragraph 37.

38. Defendants admit on information and belief that what purports to be a copy of the '630 patent is attached to the Complaint as Exhibit F. Defendants further admit that Exhibit F is titled "1-[2-(2,4-Dimethylphenylsulfanyl)-phenyl]piperazine as a Compound with Combined Serotonin Reuptake, 5-HT_3 and 5-HT_{1A} Activity for the Treatment of Cognitive Impairment" and lists January 9, 2018 as the "Date of Patent." Defendants deny all other allegations in paragraph 38.

DEFENDANTS' ANDA NO. 211146

39. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 identifies TRINTELLIX® (vortioxetine) tablets, 5 mg, 10 mg, and 20 mg, as the Reference Listed Drug. Defendants further admit that ANDA No. 211146 includes certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '884, '279, '684, '355, '946, and '630 patents. Defendants deny all other allegations in paragraph 39.

40. Defendants admit that as of April 2, 2018, FDA has not approved ANDA No. 211146. Defendants deny all other allegations in paragraph 40.

41. Defendants admit that Zydus sent the First Notice Letter dated December 14, 2017 to Lundbeck and Takeda USA pursuant to 21 U.S.C. § 355(j)(2)(B), notifying Lundbeck and Takeda USA that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), and that ANDA No. 211146 included certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '884, '279, '684, '355, and '946 patents. Defendants deny all other allegations in paragraph 41.

42. Defendants admit that Zydus sent the Second Notice Letter dated March 12, 2018 to Lundbeck and Takeda USA pursuant to 21 U.S.C. § 355(j)(2)(B), notifying Lundbeck and Takeda USA that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), and that ANDA No. 211146 was amended to include a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '630 patent. Defendants deny all other allegations in paragraph 42.

43. The allegations in the first sentence in paragraph 43 are legal conclusions to which no answer is required and do not appear to be directed to ANDA No. 211146. To the extent an answer is required, Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 includes certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '884, '279, '684, '355, '946, and '630 patents. Defendants deny all other allegations in paragraph 43.

44. The allegations in paragraph 44 are legal conclusions to which no answer is required and do not appear to be directed to ANDA No. 211146. To the extent an answer is

required, Defendants admit that Zydus has complied with applicable regulations. Defendants deny all other allegations in paragraph 44.

45. Defendants deny that the allegations in paragraph 45 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '884, '279, '684, '355, '946, and '630 patents in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 45.

46. Defendants deny that the allegations in paragraph 46 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '884, '279, '684, '355, '946, and '630 patents in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the

relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 46.

47. Defendants admit that the product labeling for the proposed product described in ANDA No. 211146 will comply with applicable law. Defendants deny all other allegations in paragraph 47.

48. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 48.

49. Denied.

50. The allegations in paragraph 50 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Zydus sent the First Notice Letter to Takeda USA and Lundbeck on December 14, 2017, and Plaintiffs filed a Complaint alleging infringement of the '884, '279, '684, '355, and '946 patents on January 25, 2018. Defendants deny all other allegations in paragraph 50.

51. Defendants admit that Plaintiffs filed the original Complaint alleging infringement of the '884, '279, '684, '355, and '946 patents on January 25, 2018 following receipt of the First Notice Letter dated December 14, 2017. Defendants further admit that Exhibit F to the Complaint purports to be a copy of the '630 patent and lists January 9, 2018 as the "Date of Patent," which is after Zydus sent the First Notice Letter dated December 14, 2017. Defendants admit that Zydus sent the Second Notice Letter dated March 12, 2018 to Lundbeck and Takeda USA pursuant to 21 U.S.C. § 355(j)(2)(B), notifying Lundbeck and Takeda USA that

ANDA No. 211146 was amended to include a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '630 patent. Defendants further admit that Plaintiffs filed the First Amended Complaint on March 19, 2018. Defendants deny all other allegations in paragraph 51.

COUNT I
INFRINGEMENT OF THE '884 PATENT

52. Defendants restate, reallege, and incorporate by reference their answers to each of the preceding paragraphs 1-51, as if fully set forth herein.

53. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 53.

54. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 54 and therefore deny them.

55. The allegations in paragraph 55 are legal conclusions to which no answer is required. To the extent an answer is required, denied.

56. The allegations in paragraph 56 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny that the allegations in paragraph 56 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '884 patent in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because

an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 56.

57. Denied.

58. Denied.

59. Denied.

60. Denied.

61. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 includes a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '884 patent. Defendants deny all other allegations in paragraph 61.

62. Denied.

63. Denied.

COUNT II
INFRINGEMENT OF THE '279 PATENT

64. Defendants restate, reallege, and incorporate by reference their answers to each of the preceding paragraphs 1-63, as if fully set forth herein.

65. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of

vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 65.

66. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 66 and therefore deny them.

67. The allegations in paragraph 67 are legal conclusions to which no answer is required. To the extent an answer is required, denied.

68. Defendants admit that the product labeling for the proposed product described in ANDA No. 211146 will comply with applicable law. Defendants deny all other allegations in paragraph 68.

69. The allegations in paragraph 69 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny that the allegations in paragraph 69 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '279 patent in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 69.

70. Denied.

71. Denied.

72. Denied.

73. Denied.

74. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 includes a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '279 patent. Defendants deny all other allegations in paragraph 74.

75. Denied.

76. Denied.

COUNT III
INFRINGEMENT OF THE '684 PATENT

77. Defendants restate, reallege, and incorporate by reference their answers to each of the preceding paragraphs 1-76, as if fully set forth herein.

78. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 78.

79. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 79 and therefore deny them.

80. The allegations in paragraph 80 are legal conclusions to which no answer is required. To the extent an answer is required, denied.

81. The allegations in paragraph 81 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny that the allegations in paragraph

81 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '684 patent in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 81.

82. Denied.

83. Denied.

84. Denied.

85. Denied.

86. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 includes a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '684 patent. Defendants deny all other allegations in paragraph 86.

87. Denied.

88. Denied.

COUNT IV
INFRINGEMENT OF THE '355 PATENT

89. Defendants restate, reallege, and incorporate by reference their answers to each of the preceding paragraphs 1-88, as if fully set forth herein.

90. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 90.

91. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 91 and therefore deny them.

92. The allegations in paragraph 92 are legal conclusions to which no answer is required. To the extent an answer is required, denied.

93. Defendants admit that the product labeling for the proposed product described in ANDA No. 211146 will comply with applicable law. Defendants deny all other allegations in paragraph 93.

94. The allegations in paragraph 94 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny that the allegations in paragraph 94 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '355 patent in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928

(BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 94.

95. Denied.

96. Denied.

97. Denied.

98. Denied.

99. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 includes a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '355 patent. Defendants deny all other allegations in paragraph 99.

100. Denied.

101. Denied.

COUNT V
INFRINGEMENT OF THE '946 PATENT

102. Defendants restate, reallege, and incorporate by reference their answers to each of the preceding paragraphs 1-101, as if fully set forth herein.

103. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 103.

104. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 104 and therefore deny them.

105. The allegations in paragraph 105 are legal conclusions to which no answer is required. To the extent an answer is required, denied.

106. Defendants admit that the product labeling for the proposed product described in ANDA No. 211146 will comply with applicable law. Defendants deny all other allegations in paragraph 106.

107. The allegations in paragraph 107 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny that the allegations in paragraph 107 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '946 patent in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 107.

108. Denied.

109. Denied.

110. Denied.

111. Denied.

112. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 includes a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '946 patent. Defendants deny all other allegations in paragraph 112.

113. Denied.

114. Denied.

COUNT VI
INFRINGEMENT OF THE '630 PATENT

115. Defendants restate, reallege, and incorporate by reference their answers to each of the preceding paragraphs 1-114, as if fully set forth herein.

116. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants deny all other allegations in paragraph 116.

117. Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 117 and therefore deny them.

118. The allegations in paragraph 118 are legal conclusions to which no answer is required. To the extent an answer is required, denied.

119. Defendants admit that the product labeling for the proposed product described in ANDA No. 211146 will comply with applicable law. Defendants deny all other allegations in paragraph 119.

120. The allegations in paragraph 120 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants deny that the allegations in paragraph 120 accurately and completely recite the Notice Letters and therefore deny them. Defendants do not waive, and expressly reserve, the right to raise additional defenses and arguments concerning noninfringement, invalidity, and unenforceability of the '630 patent in this or any ensuing litigation or other proceeding. *See Abbott Labs., Inc. v. Apotex Inc.*, 725 F. Supp. 2d 724, 728 (N.D. Ill. 2010) (refusing to strike defense theories not raised in defendant's notice letter because an ANDA filer is "not limited to the invalidity and noninfringement theories raised in its paragraph IV [notice] letter"); *Astra Aktiebolag v. Kremers Urban Dev. Co.*, No. 99 Civ. 8928 (BSJ), 2000 WL 257125, at *1 (S.D.N.Y. Mar. 8, 2000) ("There is no language in the relevant statutory provisions, legislative history or cases barring [an ANDA filer] from raising defenses and counterclaims not noticed in [its] ANDA."). Defendants deny all other allegations in paragraph 120.

121. Denied.

122. Denied.

123. Denied.

124. Denied.

125. Defendants admit that Zydus submitted ANDA No. 211146 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval to engage in the commercial manufacture, use, or sale of vortioxetine tablets, 5 mg, 10 mg, and 20 mg. Defendants further admit that ANDA No. 211146 was amended to include a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) with respect to the '630 patent. Defendants deny all other allegations in paragraph 125.

126. Denied.

127. Denied.

REQUEST FOR RELIEF

Defendants specifically deny that Plaintiffs are entitled to the general or specific relief requested against Defendants, or to any relief whatsoever, and pray for judgment in favor of Defendants dismissing this action with prejudice, and awarding Defendants their reasonable attorneys' fees pursuant to 35 U.S.C. § 285, interest, and costs of this action, and such other or further relief as this Court may deem just and proper.

AFFIRMATIVE DEFENSES

Without prejudice to the denials set forth in their Answer and without admitting any allegations of the Complaint not otherwise admitted, Defendants aver and assert the following Affirmative Defenses to Plaintiffs' Complaint.

FIRST AFFIRMATIVE DEFENSE
(Noninfringement of U.S. Patent No. 7,144,884)

Plaintiffs will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed vortioxetine tablets, 5 mg, 10 mg, and 20 mg, that are the subject of ANDA No. 211146 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the '884 patent.

SECOND AFFIRMATIVE DEFENSE
(Invalidity of U.S. Patent No. 7,144,884)

Upon information and belief, the claims of the '884 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112.

THIRD AFFIRMATIVE DEFENSE
(Noninfringement of U.S. Patent No. 8,476,279)

Plaintiffs will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed vortioxetine tablets, 5 mg, 10 mg, and 20 mg, that are the subject of ANDA No. 211146 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the ’279 patent.

FOURTH AFFIRMATIVE DEFENSE
(Invalidity of U.S. Patent No. 8,476,279)

Upon information and belief, the claims of the ’279 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112.

FIFTH AFFIRMATIVE DEFENSE
(Noninfringement of U.S. Patent No. 8,722,684)

Plaintiffs will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed vortioxetine tablets, 5 mg, 10 mg, and 20 mg, that are the subject of ANDA No. 211146 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the ’684 patent.

SIXTH AFFIRMATIVE DEFENSE
(Invalidity of U.S. Patent No. 8,722,684)

Upon information and belief, the claims of the ’684 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112.

SEVENTH AFFIRMATIVE DEFENSE
(Noninfringement of U.S. Patent No. 8,969,355)

Plaintiffs will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed vortioxetine tablets, 5 mg, 10 mg, and 20 mg, that are the subject of ANDA No. 211146 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the '355 patent.

EIGHTH AFFIRMATIVE DEFENSE
(Invalidity of U.S. Patent No. 8,969,355)

Upon information and belief, the claims of the '355 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112.

NINTH AFFIRMATIVE DEFENSE
(Noninfringement of U.S. Patent No. 9,227,946)

Plaintiffs will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed vortioxetine tablets, 5 mg, 10 mg, and 20 mg, that are the subject of ANDA No. 211146 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the '946 patent.

TENTH AFFIRMATIVE DEFENSE
(Invalidity of U.S. Patent No. 9,227,946)

Upon information and belief, the claims of the '946 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112.

ELEVENTH AFFIRMATIVE DEFENSE
(Noninfringement of U.S. Patent No. 9,861,630)

Plaintiffs will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed vortioxetine tablets, 5 mg, 10 mg, and 20 mg, that are the subject of ANDA No. 211146 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the '630 patent.

TWELFTH AFFIRMATIVE DEFENSE
(Invalidity of U.S. Patent No. 9,861,630)

Upon information and belief, the claims of the '630 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112.

RESERVATION OF DEFENSES

Defendants hereby reserve any and all defenses that are available under the Federal Rules of Civil Procedure and the U.S. Patent Laws and any other defenses, at law or in equity, that may now exist or become available later as a result of discovery and further factual investigation during this litigation.

Dated: April 2, 2018

Respectfully submitted,

By: */s/ John C. Phillips, Jr.*

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