UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

ALZHEIMER'S INSTITUTE OF AMERICA, INC.,
7837 Parallel Parkway
Kansas City, Kansas 66112,

Plaintiff,

v.

AVID RADIOPHARMACEUTICALS,
3711 Market Street, 7th Floor
Philadelphia, Pennsylvania 19104,

and

THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA,
3451 Walnut Street
Philadelphia, Pennsylvania 19104,

Defendants.

Case No.

DEMAND FOR JURY TRIAL

COMPLAINT FOR DAMAGES AND INFRINGEMENT

PLAINTIFF'S COMPLAINT

COMES NOW plaintiff Alzheimer's Institute of America, Inc. ("AIA"), by and through its attorneys, and for its Complaint against defendants Avid Radiopharmaceuticals, Inc. ("Avid") and The Trustees of the University of Pennsylvania ("University of Pennsylvania") (collectively, "Defendants"), states as follows:

Nature of the Action

1. This Complaint seeks a judgment finding that Defendants have infringed and continue to infringe upon AIA's U.S. Patent Nos. 5,455,169 (the "'169 Patent"), and 7,538,258 (the "'258 Patent") (collectively, the "Patents-in-Suit"). The Patents-in-Suit cover a wide range of Alzheimer's disease-related technology, including, but not limited to: nucleic acids coding for the Swedish mutation and transgenic mice expressing the Swedish mutation containing nucleic acids. Mice containing nucleic acid encoding for the Swedish mutation, including Tg2576 mice and APPswe-PSEN1 mice, are covered by the '169 Patent and the '258 Patent. The claimed

technology provides important insights and tools for Alzheimer's disease research. True and accurate copies of the Patents-in-Suit are attached hereto, respectively, as Exhibits A and B.

Jurisdiction and Venue

2. This Court has subject matter jurisdiction over this Complaint pursuant to 28 U.S.C. §§ 1331 and 1338(a), and under the patent laws of the United States pursuant to 35 U.S.C. § 1, *et seq.*

3. Venue is proper in this judicial district under the provisions of 28 U.S.C. §§ 1391(b) and 1400(b).

The Parties

4. AIA is a corporation organized and existing under the laws of Florida and having its principal place of business at 7837 Parallel Parkway, Kansas City, Kansas 66112. AIA is the owner of the Patents-in-Suit.

5. Avid is a Pennsylvania corporation having its principal place of business at 3711 Market Street, 7th Floor, Philadelphia, Pennsylvania 19104. Avid has committed acts of patent infringement in this district.

6. The University of Pennsylvania is a private non-profit institution having its principal place of business at the University of Pennsylvania, 3451 Walnut Street, Philadelphia, Pennsylvania 19104. The University of Pennsylvania has committed acts of patent infringement in this district.

Facts

7. Approximately 5 million people nationwide currently suffer from Alzheimer's disease. Alzheimer's disease is a neurodegenerative disease whose symptoms include memory loss, disorientation, and dementia. Alzheimer's disease is fatal.

8. Alzheimer's disease is characterized by the accumulation of aggregated Aβ or β-Amyloid peptides in senile plaques and vascular deposits.

9. AIA's patents cover a wide range of Alzheimer's disease-related technology, including, nucleic acids coding for the Swedish mutation. The Swedish mutation is a genetic mutation that results in increased amounts of β-Amyloid plaques. The Swedish mutation is used to model the effects of Alzheimer's disease for *in vitro*, *in vivo*, and animal testing.

10. Alzheimer's disease is currently diagnosed using clinical criteria, which are often inaccurate and are useful only late in the disease progression. While definitive diagnosis requires identification of amyloid plaques in the brain at autopsy, there is increasing evidence that amyloid plaques are present for many years prior to the onset of dementia.

11. Early and accurate detection of amyloid plaques by brain imaging could provide an opportunity to dramatically improve diagnosis of Alzheimer's disease and could allow monitoring of disease progression. An agent that would allow amyloid plaques to be imaged is, thus, of great commercial and medical value – both for diagnostic and drug development purposes.

12. Upon information and belief, the University of Pennsylvania was aware of the vast commercial value that such an amyloid imaging agent would have. University of Pennsylvania researchers Daniel M. Kovronsky, Bin Zhang, Mei-Ping Kung, Hank F. Kung, John Q. Trojanowski, and Virginia M-Y. Lee led the University of Pennsylvania's initial efforts to develop an amyloid imaging agent. Dr. Daniel M. Skovronsky served as Scientific Director of High Throughput Screening and Drug Discovery at the Center for Neurodegenerative Disease Research at the University of Pennsylvania. Dr. Hank F. Kung served as served as Professor of Radiology and Pharmacology.

13. On June 20, 2000, the University of Pennsylvania published the results of its "first step" towards the development of such an amyloid imaging agent in the *Proceedings for National Academy of Sciences*, Vol. 97, No. 13, pp. 7609-7614 (June 20, 2000). As described in the publication, the University of Pennsylvania developed a fluorescent probe known as [(trans, trans)-1-bromo-2,5-bis-(3-hydroxycarbonyl-4-hydroxy)styrylbenzene or "BSB" for short. Prior to this publication entitled, "*In vivo* detection of amyloid plaques in a mouse model of

Alzhiemer's disease," no probe had been shown to label senile or amyloid plaques *in vivo*, which is required of a ligand used for imaging plaques in Alzheimer's disease patients.

14. To determine whether BSB could label amyloid plaques *in* vivo, the University of Pennsylvania used a transgenic mouse strain known as Tg2576. The Tg2576 mouse contains nucleic acids encoding for amyloid precursor protein with the Swedish mutation. Due to the presence of the Swedish mutation, the Tg2576 mice over produce β-Amyloid, develop β-Amyloid plaques, and demonstrate symptoms consistent with Alzheimer's disease. Because the Tg2576 mice contain nucleic acids encoding for amyloid precursor protein with the Swedish mutation, a license from AIA is required to use the Tg2576 mice. Without a license, use of the Tg2576 mice is an infringement of the '169 Patent and the '258 Patent.

15. The University of Pennsylvania was not authorized to use the Tg2576 mice for profit-making or commercial purposes. The University of Pennsylvania understood that its use of the Tg2576 mice in developing an amyloid imaging agent was a commercial purpose.

16. As a direct result of its use of the Tg2576 mice, the University of Pennsylvania concluded that "BSB is an appropriate starting point for future efforts to generate an antemortem diagnostic for AD [Alzheimer's disease]" and that "BSB can serve as a useful prototype ligand for developing probes to establish a diagnosis of AD in living patients." In particular, the University of Pennsylvania determined that "BSB has several properties that suggest that BSB or a BSB-like derivative may become a useful probe for imaging AD pathology *in vivo*: (i) BSB labels Aβ amyloid plaques specifically and sensitively; (ii) BSB is cell permeable; (iii) BSB distributes through the brain after a single intracerebral injection; (iv) after binding to plaques, BSB is stable *in vivo*; and (v) BSB cross the BBB [blood brain barrier] of transgenic mouse models of AD amyloidosis and labels Aβ deposits."

17. Between 2000 and 2005, the University of Pennsylvania continued to use the Tg2576 mice to identify, validate, and test potential amyloid imaging agents. For example, in June 2002, the University of Pennsylvania described the use of the Tg2576 mice in testing of compounds known as [^{125}I]IMSB and [^{125}I]TZDM, which showed a 10-fold greater brain

penetration compared to BSB. In addition, these radiolabeled probes labeled plaques with higher sensitivity for *in vivo* imaging in contrast to fluorescent probes like BSB, which require exposure of the brain to microscopy.[1] Radiolabeled probes may be imaged using positron emission computed tomography (PET) or single photon emission computed tomography (SPECT) imaging. In addition, the University of Pennsylvania used Tg2576 mice to identify and validate the radiolabeled compound known as [^{125}I]IMPY as a potential amyloid imaging agent.[2]

18. In late 2004, Dr. Skovronsky and Dr. Kung founded defendant Avid. Upon information and belief, Avid was designed to commercialize and monetize the discoveries made at the University of Pennsylvania. Dr. Skovronsky is the CEO and a shareholder of Avid. Dr. Kung is a scientific advisor and shareholder of Avid. Avid licensed certain technology from the University of Pennsylvania that was discovered by using AIA's patented technology.

19. According to its website, "Avid's Alzheimer's disease program is based on the hypothesis that *in vivo* detection of amyloid plaques by positron emission computed tomography (PET) or single photon emission computed tomography (SPECT) imaging will be useful as biomarkers for monitoring and diagnosis of Alzheimer's disease. In collaboration with Dr. Hank Kung at the University of Pennsylvania, we have developed novel radiolabeled compounds that specifically and sensitively bind β-amyloid (the chief constituent of amyloid plaques) and are testing these compounds as molecular imaging agents in preclinical and clinical trials."

20. Since Avid's founding, Avid and the University of Pennsylvania have collaborated in the identification, validation, testing, and commercialization of amyloid imaging agents.[3] The collaboration between Avid and the University of Pennsylvania included the

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1 *See* M.-P. Kung, et al., "Detection of Amyloid Plaques by Radioligands for Aβ40 and Aβ42," *Journal of Molecular Neuroscience*, Vol. 20, pp. 15-23 (2003).

2 *See* H.F. Kung, et al., "Iodinated Traces for Imaging Amyloid Plaques in the Brain," *Molecular Imaging and Biology*, Vol. 5, No. 6, pp. 418-426 (2003).

3 *See, e.g.*, A. B. Newberg, et al., "Safety, Biodistribution, and Dosimetry of ^{123}I-IMPY: A Novel Amyloid Plaque-Imaging Agent for the Diagnosis of Alzheimer's Disease," *The Journal of Nuclear Medicine*, Vol. 47, No. 5, pp. 748-754 (May 2006); C. C. Rowe, et al., "Imaging of amyloid β in Alzheimer's disease with ^{18}F-BAY94-9172, a novel PET tracer: proof of mechanism," *The Lancet: Neurology*, Vol. 7, pp. 129-135 (February 2008); W. Qu, et al.,

continued use of the Tg2576 mice and other mice containing nucleic acids encoding for amyloid precursor protein with the Swedish mutation.

21. For example, in C. C. Rowe, et al., "Imaging of amyloid β in Alzheimer's disease with ^{18}F-BAY94-9172, a novel PET tracer: proof of mechanism," *The Lancet: Neurology*, Vol. 7, pp. 129-135 (February 2008), Avid and the University of Pennsylvania report that "[a]fter injection into Tg2576 transgenic mice, *ex vivo* brain sections showed localization of ^{18}F-BAY94-9172 in regions with Aβ plaques as confirmed by thoflavin binding."

22. In November 2009, Avid and the University of Pennsylvania jointly reported on the properties of an amyloid imaging agent known as ^{18}F-AV-45. *See* S.R. Choi, et al., "Preclinical Properties of ^{18}F-AV-45: A PET Agent for Aβ Plaques in the Brain," *The Journal of Nuclear Medicine*, Vol. 50, No. 11, pp. 1887-1894 (November 2009). In particular, they reported that "^{18}F-AV-45 displayed excellent binding affinity to Aβ plaques in the AD brain by *ex vivo* autoradiography in transgenic AD model mice." The transgenic AD model mice used by Avid and the University of Pennsylvania included mice known as B6 Cg-Tg APPswe-PSEN1.

23. According to the publication, Avid and the University of Pennsylvania purchased the B6 Cg-Tg APPswe-PSEN1 mice from The Jackson Laboratory. The Jackson Laboratory sells these APPswe-PSEN1 mice as stock number 004462. The APPswe-PSEN1 mice infringe the Patents-in-Suit. The sale of the APPswe-PSEN1 mice was not authorized by AIA. The use of the APPswe-PSEN1 mice by Avid and the University of Pennsylvania was not authorized by

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"Synthesis and evaluation of indoliny- and indolylphenylacetylenes as PET imaging agents for β-amyolid plaques," *Bioorg. Med. Chem. Lett.*, Vol. 18, No. 17, pp. 4823-4827 (September 2008); S.-P. Wey, et al., "Validation of an ^{18}F-labeled biphenyalkyne as a positron emission tomography imaging agent for β-amyloid plaques," *Nuclear Medicine and Biology*, Vol. 36, pp. 411-417 (2009); H. F. Kung, et al., "^{18}F Stilbenes and Styrylpyridines for PET Imaging of Aβ Plaques in Alzheimer's Disease: A Miniperspective," *Journal of Medicinal Chemistry*, Vol. 53, No. 3, pp. 933-941 (2010); C.-H. Yao, et al., "GMP-compliant automated synthesis of [^{18}F]AV-45 (Florbetapir F 18) for imaging β-amyolid plaques in human brain," *Applied Radiation and Isotopes*, Vol. 68, pp. 2293-2297 (2010); D. F. Wong, et al., "In Vivo Imaging of Amyolid Deposition in Alzheimer Disease Using the Radioligand ^{18}F-AV-45 (Florbetapir F 18)," *The Journal of Nuclear Medicine*, Vol. 51, No. 6, pp. 913-920 (June 2010); K.-J. Lin, et al., "Whole-body biodistribution and brain PET imaging with [^{18}F]AV-45. a novel amyloid imaging agent – a pilot study," *Nuclear Medicine and Biology*, Vol. 37, pp. 497-508 (2010).

AIA. Without a license, use of the APPswe-PSEN1 mice is an infringement of the '169 Patent and the '258 Patent.

24. The Jackson Laboratory prominently announces on its website and in the Terms of Use it sends with the APPswe-PSEN1 mice that the APPswe-PSEN1 strain of mice is "not available to companies or for-profit entities" and that "use of these MICE for Commercial Purposes is strictly prohibited." Avid and the University of Pennsylvania knew or should have known that the commercial use of the APPswe-PSEN1 mice was not authorized.

25. Defendant Avid describes itself as "a pioneer in the development of agents for diagnosis of Alzheimer's disease." According to its website, Avid "has developed proprietary targeting agents to image β-Amyloid plaques and is currently testing these compounds in clinical trials for the detection of Alzheimer's disease." One such imaging agent, ^{18}F-AV-45, is currently in Phase III clinical trials as part of the FDA approval process.

26. The imaging agents that Avid and the University of Pennsylvania have identified, validated, and tested using AIA's patented technology are extremely valuable. The University of Pennsylvania has filed applications for, and obtained, patents with the United States Patent and Trademark Office, including U.S. Patent Nos. 6,696,039; 6,946,116; 7,250,525; 7,297,820; 7,425,318; 7,678,819; 7,687,052; 7,759,502; and 7,807,135, in which the University of Pennsylvania claims certain amyloid imaging agents that were identified, validated, and tested using AIA's patented technology. The University of Pennsylvania has licensed certain of these applications and patents to Avid.

27. According to its website, Avid has raised at least $69.5 million dollars in financing since 2006. In addition, Avid has entered into an exclusive option agreement with Bayer Schering Pharma for the development of certain of these amyloid imaging agents, including ^{18}F-BAY94-9172.

28. In April 2010, Avid reported positive interim results from the Phase III clinical trial of its amyloid imaging agent Florbetapir F18, also known as ^{18}F-AV-45, stating that the

"early data show strong correlation between Florbetapir PET imaging and Alzheimer's disease beta-amyloid pathology as assessed at autopsy."

29. As of October 2010, Avid has completed its Phase III study on Florebetapir F18.

30. On November 8, 2010, Eli Lilly and Company ("Lilly") announced that it had signed a definitive merger agreement to acquire Avid. Lilly stated that "Avid's lead program in development is Florbetapir F 18 (^{18}F-AV-45), a molecular imaging agent under investigation for detecting the presence of amyloid plaque in the brain. Beta-amyloid plaque is a defining pathology of Alzheimer's disease. A marketing application for Florbetapir has recently been submitted to the U.S. Food and Drug Administration (FDA)." According to Lilly's press release, Lilly will acquire all outstanding shares of Avid for an upfront payment of $300 million, subject to adjustment based on existing cash on hand at closing. In addition, Avid shareholders, including Dr. Skovronsky and Dr. Kung, will also be eligible for up to $500 million in additional payments contingent upon potential future regulatory and commercial milestones for Florbetapir.

31. On November 17, 2010, AIA sent a letter to Defendants informing Defendants that AIA believed Defendants were infringing on AIA's patented technology. AIA requested that Defendants provide AIA with the legal basis for their prior and apparent continuing use of AIA's patents. Defendants' deadline to respond to the letter was November 24, 2010. As of the filing of this Complaint, AIA had not received a response from Defendants.

COUNT I

Patent Infringement of U.S. Patent No. 5,455,169

32. AIA incorporates by reference each and every allegation set forth in paragraphs 1 through 31 of its Complaint as if fully set forth and restated herein.

33. The '169 Patent entitled "Nucleic acids for diagnosing and modeling Alzheimer's disease" was duly and regularly issued on October 3, 1995. AIA is the sole and exclusive owner of the '169 Patent. At all relevant times, the owner of the '169 Patent has complied with 35 U.S.C. § 287(a).

34. Defendants, without the authority or consent of AIA, have used in the United States, including, but not limited to, in this judicial district, technologies which infringe upon the '169 Patent. Upon information and belief, Defendants' infringement of the '169 Patent is knowing and willful.

35. Avid's and the University of Pennsylvania's infringement of the '169 Patent has caused and continues to cause damage to AIA. Among other remedies, AIA is entitled to a reasonable royalty that includes a percentage of the expected sales of Florbetapir and other compounds that were identified, validated, and tested using AIA's patented technology.

COUNT II

Patent Infringement of U.S. Patent No. 7,538,258

36. AIA incorporates by reference each and every allegation set forth in paragraphs 1 through 35 of its Complaint as if fully set forth and restated herein.

37. The '258 Patent entitled "Transgenic mouse expressing an APP 670/671 mutation" was duly and regularly issued on May 26, 2009. AIA is the sole and exclusive owner of the '258 Patent. At all relevant times, the owner of the '258 Patent has complied with 35 U.S.C. § 287(a).

38. Defendants, without the authority or consent of AIA, have used in the United States, including, but not limited to, in this judicial district, technologies which infringe upon the '258 Patent. Upon information and belief, Defendants' infringement of the '258 Patent is knowing and willful.

39. Avid's and the University of Pennsylvania's infringement of the '258 Patent has caused and continues to cause damage to AIA. Among other remedies, AIA is entitled to a reasonable royalty that includes a percentage of the expected sales of Florbetapir and other compounds that were identified, validated, and tested using AIA's patented technology.

PRAYER

WHEREFORE, plaintiff Alzheimer's Institute of America respectfully prays that the Court enter judgment in its favor and award the following relief against Defendants:

A. Find that Defendants infringed upon the Patents-in-Suit;

B. Find that the infringement of Defendants upon the Patents-in-Suit was knowing and willful;

C. Enjoin Defendants and their respective officers, directors, employees, agents, licensees, representatives, affiliates, related companies, servants, successors and assigns, and any and all persons acting in privity or in concert with any of them, preliminarily and permanently, from further infringing upon the Patents-in-Suit;

D. Order that an accounting be made to establish damages arising out of Defendants' infringement of the Patents-in-Suit;

E. Award AIA actual damages pursuant to 35 U.S.C. § 284 in an amount to be determined at trial as a result of Defendants' infringement upon the Patents-in-Suit;

F. Award AIA treble damages pursuant to 35 U.S.C. § 284 in an amount to be determined at trial as a result of Defendants' knowing and willful infringement upon the Patents-in-Suit;

G. Award AIA its costs and reasonable attorneys' fees incurred in connection with this action; and

H. Award and grant AIA such other and further relief as the Court deems just and proper under the circumstances.

DEMAND FOR JURY TRIAL

Plaintiff demands a jury trial.

Dated: November 24, 2010

FOX ROTHSCHILD LLP

By: _____

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