IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

VANDERBILT UNIVERSITY 2201 West End Avenue Nashville, Tennessee 21060-6401	*	
Plaintiff,	*	**Case No:**
v.	*	Jury of Twelve Demanded
ICOS CORPORATION 22021 Twentieth Avenue, S.E. Bothell, Washington 98021	*	
Defendant.	*	

* * * * * * * * * * * * *

COMPLAINT FOR CORRECTION OF NAMED INVENTOR
ON U.S. PATENTS NOS. 5,859,006 AND 6,140,329

Plaintiff, The Vanderbilt University ("Vanderbilt"), by and through its undersigned attorneys, pursuant to 35 U.S.C. Section 256, hereby sues ICOS Corporation ("ICOS"), owner, by assignment, of U.S. Patents Nos. 5,859,006 and 6,140,329 and, for the reasons set forth below, requests that the Court order the Commissioner of Patents and Trademarks of the United States Patent and Trademark Office to correct the patents by adding Jackie Corbin, PhD, Sharron Francis, PhD, and Sekhar Raja Konjeti, PhD, as a co-inventors.

Nature of the Action

1. Vanderbilt scientists Jackie D. Corbin, PhD, Sharron H. Francis, PhD, and Sekhar Raja Konjeti, PhD each contributed to the conception of the inventions reflected in U.S. Patents Nos. 5,859,006 and 6,140,329, yet, through omission, inadvertence and/or error, were not named as co-inventors with Alain Daugan when the applications, that matured into those patents, were filed by GLAXO/France Corp. ("GLAXO"), nor before the patents issued naming ICOS as

assignee thereof. Vanderbilt, as assignees of Drs. Corbin, Francis and Konjeti's rights as co-inventors, request that the Court order the Commissioner of Patents and Trademarks of the U.S. Patent and Trademark Office to correct the Patents to add them as co-inventors.

The Parties

2. Vanderbilt is a Tennessee not-for-profit corporation with its principal place of business in Nashville, Davidson County, Tennessee.

3. ICOS is a corporation organized under the laws of the State of Delaware with its principal place of business located at 22021 Twentieth Avenue, S.E., Bothell, Washington 98021.

Jurisdiction and Venue

4. This action is brought under 35 U.S.C. § 256 and thus the Court has subject matter jurisdiction over this matter under 28 U.S.C. §§ 1331 and 1338.

5. At all times relevant herein, ICOS was incorporated in the State of Delaware. This Court therefore has personal jurisdiction over ICOS.

6. The venue of this action is properly found in this Court, pursuant to 28 U.S.C. §§ 1391(b) and (c) because ICOS is subject to personal jurisdiction in this District.

Factual Background

PDE-5

7. Phosphodiesterases (PDEs) are a family of closely related enzymes produced by the human body, each of which controls or regulates the function of various parts of the body. It has long been a desire of medical science to selectively enhance or inhibit the activities of these various PDEs, depending upon the therapeutic or medicinal effect desired. Designing chemical compounds that will have the desired effect on particular PDEs has proven to be extremely

difficult. In the past, much hit or miss experimentation was required to ascertain the identity of successful enhancers (agonists) or inhibitors (antagonists) of particular PDEs. The process of identification of successful agonists/antagonists is complicated by the fact that most, if not all, of the PDEs are very similar in structure and in the way they interact with potential agonists or antagonists. Therefore, it is very difficult to define an inhibitor that is specific to one PDE type that does not also affect some other PDE type, thereby compromising its usefulness as an inhibitor by, among other things, producing unwanted side effects.

8. Cyclic guanosine monophosphate ("cGMP") is a nucleotide produced by smooth muscle tissues in the body and which relaxes those tissues. In blood vessels, the relaxation of vascular smooth muscles caused by cGMP leads to increased blood flow. Such increased blood flow is an important component of such physiological events as penile erection.

9. The phosphodiesterase,PDE type 5 ("PDE-5"), is known to attach to and degrade cGMP, thereby abrogating its effect on smooth muscle tissue.

10. Given the potential therapeutic effects of increased blood flow with respect to cardiovascular disease and erectile dysfunction, researchers have focused on developing agents that will specifically inhibit the ability of PDE-5 to degrade cGMP.

11. Jackie D. Corbin, PhD ("Dr. Corbin") has served as a professor in the Department of Molecular Physiology & Biophysics in the Vanderbilt University School of Medicine since 1980. He served in the same department as an assistant professor from 1971 to 1975 and as an associate professor from 1975 to 1980. He has devoted much of his nearly 40 year career, including especially the last 20 years, to the study of cyclic nucleotides and phosphoproteins, and has written and lectured extensively on phosphodiesterases and cGMP. A copy of Dr. Corbin's curriculum vitae is attached hereto as Exhibit A.

12. Sharron H. Francis, PhD ("Dr. Francis") has served has served from 1990-1995 as Research Associate Professor in the Department of Molecular Physiology and Biophysics in the Vanderbilt University School of Medicine and as Research Professor in the Department of Molecular Physiology and Biophysics in the Vanderbilt University School of Medicine from 1996 to the present. From 1975-1989 she was Assistant Professor in the Department of Molecular Physiology and Biophysics in the Vanderbilt University Medical School, where she did rigorous research into the regulatory and catalytic mechanisms of enzymes involved in cyclic nucleotide mechanism. The primary focus of her research was the cGMP-binding phosphodiesterase, and the involvement of these enzymes in the regulation of smooth muscle tone. From 1979-1984, Dr. Francis was Director of Core Laboratory for Diabetes Endocrinology Research Training Center at Vanderbilt. From 1984-1989 she was Associate of the Howard Hughes Medical Institute at Vanderbilt. A copy of Dr. Francis's curriculum vitae is attached hereto as Exhibit B.

13. Sekhar Raja Konjeti, PhD ("Dr. Konjeti") has served as a professor (both Associate and Assistant) and a Research Instructor in the Department of Radiation Oncology in the Vanderbilt University School of Medicine since 1995. He was a Research Associate in the Department of Molecular Physiology & Biophysics in the Vanderbilt University School of Medicine from 1990 to 1995. From 1984 to 1989, Dr. Konjeti was a graduate student, exchange scientist and senior research fellow, respectively, at Gulbarga University in India, University of Sunderland in England and Gulbarga University. A copy of Dr. Konjeti's curriculum vitae is attached hereto as Exhibit C.

14. As early as 1979, Drs. Corbin and Francis concluded that critical to the conception of an effective PDE-5 inhibitor was the ability to produce pure PDE-5 for testing and drug testing purposes.

15. In 1989 Drs. Corbin obtained a research grant from Glaxo, Inc. for the purpose of research and development of cGMP analogs, including research regarding the interaction of the analogs with PDE-5. A copy of the related research agreement, on which Dr. Corbin is identified as the "Principal Investigator," is attached hereto as Exhibit D.

16. In 1988-1989, the Corbin/Francis group, with the collaboration of their Vanderbilt graduate student, Melissa Thomas, and while working under the Glaxo research agreement, succeeded in determining from bovine PDE-5 an amino acid sequence critical for cloning the cDNA of the enzyme. Discovery of that critical amino acid sequence made it possible to subsequently obtain bovine and human PDE-5 and constituted the conception of said clones to obtain recombinant PDE-5 for inhibitor testing and screening purposes. The critical amino acid sequence was taken by another of their Vanderbilt graduate students, Linda McAllister, to the University of Washington where she used it to screen a cDNA library in order to obtain the bovine PDE-5 cDNA. The University of Washington subsequently turned that information and recombinant PDE-5 cDNA over to ICOS. With these in hand it became a simple matter for ICOS to create recombinant PDE-5 enzyme

17. In 1992, just prior to the expiration of the 1989 research agreement, Vanderbilt executed a follow-on research agreement with Glaxo Group Research Ltd. A copy of the 1992 Agreement is attached hereto as Exhibit E. The introduction to the attached description of the research pointed out that

> During the tenure of our current Glaxo Cardiovascular Discovery project, we have developed a diverse catalog of highly potent cGMP analogs for relaxing vascular

> smooth muscle, which surpass the potencies of those previously available (see enclosed manuscript by Sekhar, et al.). These new compounds have provided for important new insights into the basic mechanisms of regulation of the protein kinases as well as into their involvement in relaxation. **It is anticipated that some of the compounds generated by this project, and by future projects, will be used by Glaxo scientists at various international sites** for intact tissue and animal testing as well as for other experiments. It is well-known from the work of many groups, including our own, that the **cGMP-dependent protein kinase** (cG Kinase) **has important disease-related functions** other than the induction of vascular smooth muscle relaxation. **These include** airway smooth muscle relaxation (asthma), **corpus cavernosum relaxation (male impotence)**, and platelet aggregation inhibition (cardiovascular malfunction). Additionally, four groups have reported within the last year that nerve cell long-term potentiation memory) is mediated by cGMP. **Our cGMP analogs and phosphodiesterase (PDE) inhibitors are likely to be effective in many of these systems.**

Exhibit C, p. 12 (Emphasis supplied). The two primary focuses of the research were identified as cGMP analogs and "Inhibitors of a cGMP-Binding PDE." Of the latter the description sets forth the Vanderbilt group's theory that the potencies of such inhibitors could be enhanced if they could be constructed to mimic the cGMP molecule. *See* Exhibit E, p. 14.

18. As with the earlier research agreement, the 1992 Agreement required Vanderbilt to report the results of its research to Glaxo on a regular basis. *See* Exhibit E, p. 6. Among the many Glaxo scientists with whom Vanderbilt shared the results of its research were several, including Pascal Grondin, of the Laboratoire GlaxoSmithKline, Centre de Recherches, in France.

19. In 1994, unbeknownst to the Vanderbilt scientists, Glaxo filed an application in the United States Patent and Trademark Office for a patent for a PDE-5 inhibitor identifying as its sole inventor Alain Daugan of the French Glaxo lab. That patent, No. 5,859,006, was issued on January 12, 1999.

20. In 1995, unbeknownst to the Vanderbilt scientists, Glaxo filed an application to the United States Patent and Trademark Office for a patent for the use of certain PDE-5

inhibitors to treat male impotence, again identifying as the sole inventor Alain Daugan of the French Glaxo lab. That patent, No. 6,140,329, was issued on October 31, 2000.

21. In 2003, Daugan, together with Pascal Grondin and six other scientists from the French Glaxo lab, published a series of articles in the Journal of Medicinal Chemistry entitled *The Discovery of Tadalafil*. It is readily and undeniably apparent from those articles that the French Glaxo team employed the results of the Vanderbilt team's research in the conception of Tadalafil, and, in using recombinant human cGMP to test the inhibitor, taking advantage of the amino acid sequence that Vanderbilt's scientists had discovered and used to clone recombinant bovine PDE-5. And, as set forth in the description of the research description appended to the 1992 Agreement, it was the Vanderbilt scientists that had first conceived that a PDE-5 inhibitor derived following their suggestions would be effective in treating male impotency. However, through omission, inadvertence and/or error, Glaxo failed to list Drs. Corbin, Konjeti or Francis as co-inventors in the applications for Patents Nos. 5,859,006 and 6,140,329.

22. Upon information and belief, Glaxo, assignee from Alan Daugan of the rights in Patents 5,859,006 and 6,140,329, assigned those rights to ICOS.

Count I

Correction of Named Inventor
On U.S. Patent No. 5,859,006

23. The allegations of paragraphs 1 through 22 of this Complaint are repeated, re-alleged and incorporated herein as if fully set forth in this Count.

24. Drs. Corbin, Konjeti, and Francis each made independent conceptual contributions to the inventions described in claims 1-8, 10, and 12-13 of Patent 5,859,006, and those contributions were communicated to and shared with Glaxo prior to the application for that patent.

25. Through omission, inadvertance and/or error, Drs. Corbin, Konjeti, and Francis were not identified as co-inventors of those inventions on that application, and, as a result, they do not appear as co-inventors on the corresponding Letters of Patent issued by the United States Patent and Trademark Office.

WHEREFORE, as to Count I of this Complaint, Vanderbilt respectfully requests that the Court issue an order directing the Commissioner of Patents and Trademarks of the United States Patent and Trademark Office to correct Patent No. 5,859,006 by adding Jackie Corbin, PhD, Sharron Francis, PhD, and Sekhar Raja Konjeti, PhD, as a co-inventors thereon.

Count II

Correction of Named Inventor
On U.S. Patent No. 6,140,329

26. The allegations of paragraphs 1 through 25 of this Complaint are repeated, re-alleged and incorporated herein as if fully set forth in this Count.

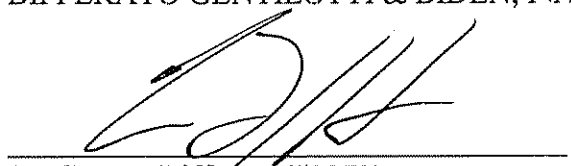
27. Drs. Corbin, Konjeti, and Francis each made independent conceptual contributions to the inventions described in claims 1-3, 5-12, and 15-21of Patent 6,140,329, and those contributions were communicated to and shared with Glaxo prior to the application for that patent.

28. Through omission, inadvertence, and/or error, Drs. Corbin, Konjeti, and Francis were not identified as co-inventors of those inventions on that application and, as a result, they do not appear as co-inventors on the corresponding Letters of Patent issued by the United States Patent and Trademark Office.

WHEREFORE, as to Count II of this Complaint, Vanderbilt respectfully requests that the Court issue an order directing the Commissioner of Patents and Trademarks of the United States

Patent and Trademark Office to correct Patent No. 6,140,329 by adding Jackie Corbin, PhD, Sharron Francis, PhD, and Sekhar Raja Konjeti, PhD, as a co-inventors thereon.

BIFFERATO GENTILOTTI & BIDEN, P.A



Ian Connor Bifferato (#3273)
Vincent A. Bifferato, Jr. (#2465)
Joseph R. Biden, III (#4203)
Joseph K. Koury (#4272)
Bifferato, Gentilotti & Biden, P.A.
1308 Delaware Avenue
Wilmington, Delaware 19806

and

Kurt C. Rommel
Miles & Stockbridge P.C.
1751 Pinnacle Drive, Suite 500
McLean, Virginia 22102-3833

and

Robert S. Brennen
Donald E. English, Jr.
Aaron C. Storm
Miles & Stockbridge P.C.
10 Light Street
Baltimore, Maryland 21202
(410) 727-6464

[*Remainder of Page Intentionally Left Blank*]

and

Leona Marx
University Counsel
Vanderbilt University
Office of the General Counsel
Suite 750, Loews Vanderbilt Plaza
2100 West End Avenue
Nashville Tennessee 37203

Attorneys for Plaintiff,
Vanderbilt University

964608