4 October 2011

President Ruth J. Simmons
Office of the President
Brown University
1 Prospect Street
Campus Box 1860
Providence, Rhode Island 02912

Dear President Simmons,

Study 329: A multi-center, double blind, placebo controlled study of paroxetine and imipramine in adolescents with unipolar major depression

We write to you about our ongoing concerns regarding a journal article that originated at the Department of Psychiatry and Human Behavior, under the leadership of Dr. Martin Keller.

Between 1993 and 1998, SmithKline Beecham (subsequently GlaxoSmithKline) provided $800,000 to Brown University for its participation in the above study.[1] The results were published in 2001 by Keller et al. in a journal article, 'Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial',[2] in the *Journal of the American Academy of Child & Adolescent Psychiatry*.

The article was ghostwritten by agents of the manufacturer, and seriously misrepresented both the effectiveness and the safety of paroxetine in treating adolescent depression.

While problems with study 329 and the Keller et al paper have been thoroughly exposed in legal actions,[3] the bioethical and medical literature,[4] a book,[5] and a BBC Panorama documentary[6], the paper continues to be cited uncritically in the medical literature as evidence of the efficacy of paroxetine for treatment of adolescent depression.[7],[8] Our main concern is that adolescents are being harmed because well-intentioned physicians have been misled.

Moreover, the misrepresentation has been compounded by the following:
1) The *Journal* was asked by two of the undersigned, Drs. Jureidini and McHenry, to retract the article, but has refused to do so.
2) In a letter of May 13, 2008, from Pamela D. Ring to Dr. David Egilman, Brown University refused to release information about its internal investigation into Dr. Keller's conflicts of interest and scientific misconduct.

Study 329 reveals the pervasive influence of GlaxoSmithKline's marketing objectives on the preparation and publication of a 'scientific' manuscript and peer-reviewed journal article. GlaxoSmithKline's own internal documents disclosed in litigation show that company staff were aware that the study 329 did not support a claim of efficacy but decided that it would be "unacceptable commercially" to reveal that.[9]

The data were therefore selectively reported in Keller *et al*.'s article, in order to "effectively manage the dissemination of these data in order to minimise any potential negative commercial impact".[9] As it turns out, the Keller *et al*. article was used by GlaxoSmithKline's to ward off potential damage to the profile of paroxetine and it was used to promote off-label

prescriptions of Paxil® and Seroxat® to children and adolescents, some of whom became suicidal and self-harmed as a result.[10]

The unretracted article is a stain on Brown University's reputation for academic excellence. The University cannot claim to be a leader in scientific research and moral integrity while failing to act to redress this article that negligently misrepresents scientific findings.

In its accreditation document for the New England Association of Schools and Colleges (NEASC), Brown University claims in relation to 'Standard Eleven: Integrity' that 'The institution manages its academic, research and service programs, administrative operations, responsibilities for students and interactions with prospective students with honesty and integrity', that it 'expects that members of its community, including the board, administration, faculty, staff, and students, will act responsibly and with integrity', and that 'Truthfulness, clarity, and fairness characterize the institution's relations with all internal and external constituencies'.[11] The University's inaction in relation to study 329 casts doubt on the validity of these claims.

We ask that you write to the editor, Dr. Andrés Martin, *Journal of the American Academy of Child & Adolescent Psychiatry* supporting our request for retraction of the journal article.

We are making this letter available to interested parties and it will be posted on the Healthy Skepticism website (www.healthyskepticism.org).

Yours sincerely

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Jim Wright
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Liliya E. Ziganshina
Head, Professor, Department of Basic and Clinical Pharmacology, Kazan Federal University, Russian Federation

[1] Keller M. (2011). Martin B. Keller, MD. Providence, RI: Brown University; 2011. http://research.brown.edu/pdf/1100924449.pdf

[2] Keller MB, Ryan ND, Strober M, Klein RG, Kutcher SP, Birmaher B, Hagino OR, Koplewicz H, Carlson GA, Clarke GN, Emslie GJ, Feinberg D, Geller B, Kusumakar V, Papatheodorou G, Sack WH, Sweeney M, Wagner KD, Weller EB, Winters NC, Oakes R, McCafferty JP. Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2001 Jul;40(7):762-72.

[3] *The People of the State of New York vs. SmithKline Beecham Corp.* (Case No. 04-CV-5304 MGC), *Beverly Smith vs. SmithKline Beecham Corp.* (Case No. 04 CC 00590), *Engh vs. SmithKline Beecham Corp*. (Case No. PI 04-012879), *Teri Hoormann vs. SmithKline Beecham Corp.* (Case No. 04-L-715) and *Julie Goldenberg and Universal Care vs. SmithKline Beecham Corp.* (Case No. 04 CC 00653)

[4] Jureidini JN, McHenry LB, Mansfield PR. Clinical trials and drug promotion: selective reporting of study 329. *Int J Risk Saf Med* 2008;20:73-81. http://www.pharmalot.com/wp-content/uploads/2008/04/329-study-paxil.pdf

[5] Bass A. Side effects: A prosecutor, a whistleblower, and a bestselling antidepressant on trial. Chapel Hill, NC: Algonquin Books; 2008.

[6] BBC. Seroxat – Secrets of the Drugs Trials. Panorama. BBC one; 2007 Jan 29. http://news.bbc.co.uk/2/hi/programmes/panorama/6291773.stm

[7] http://scholar.google.com.au/scholar?hl=en&lr=&cites=7589903240306694483

[8] Jureidini J, McHenry L. Conflicted medical journals and the failure of trust. Accountability in Research 18:45-54.

[9] SmithKline Beecham, Seroxat/Paxil adolescent depression position piece on the Phase III clinical studies, October 1998, PAR003019178; http://www.healthyskepticism.org/documents/documents/19981014PositionPiece.pdf

[10] Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry. 2006 Mar;63(3):332-9

[11] Brown University. Standard Eleven: Integrity. NEASC Accreditation; 2008. http://www.brown.edu/Project/NEASC/Standards/integrity_11.php