ONLINE APPENDIX

I. List of Study Site Investigators

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Dr. Francis Agnone Phoenix AZ (9), Dr. Meera Amar Waco TX (13)

Dr. Corey Anderson Sun City AZ (65), Dr. Harold Bays Louisville KY (30)

Dr. Bruce Bowling Endwell NY (72), Dr. Paul Bristol Austin TX (16)

Dr. Dennis Buth Wichita KS (49), Dr. Jambur Chandrashekar Indio CA (15)

Dr. Teresa Coats Austin TX (5), Dr. Pankaj Desai Owings Mills MD (15)

Dr. John Earl Hickory NC (76), Dr. Philip Emrie Wheat Ridge CO (2)

Dr. John Ervin Kansas City MO (48), Dr. Cecil Farrington Salisbury NC (123)

Dr. R. David Ferrera Sacramento CA (30), Dr. Jerome Fischer San Antonio TX (81), Dr. Steven Folkerth Las Vegas NV (10), Dr. Neil Fraser Troy MI (41)

Dr. Lawrence Gassner Phoenix AZ (7), Dr. Carl Griffin Oklahoma City OK (11)

Dr. Charles Herring Wilmington NC (157), Dr. Darrell Herrington San Angelo TX (35), Dr. Stephen Hippler Peoria IL (14), Dr. Harry Larkin Ship Bottom NJ (19)

Dr. Kurt Lesh Colorado Springs CO (54), Dr. James Lieber Chandler AZ (9)

Dr. Timothy Linder Selmer TN (9), Dr. Thomas Littlejohn III Winston-Salem NC (152), Dr. N. Martin Lunde Brooklyn Center MN (37), Dr. Scott Meyers Wichita KS (77), Dr. Richard Mills Mt. Pleasant SC (66), Dr. Manuel Modiano Tucson AZ (33), Dr. David Morin Bristol TN (97), Dr. Julio Pagan Dyersberg TN (4)

Dr. James Payne Jackson TN (3), Dr. Geri Poss San Antonio TX (10)

Dr. George Raad Charlotte NC (103), Dr. Patrick Rask Portland OR (9)

Dr. Marc Rendell Omaha NE (53), Dr. L. Edward Roberts, Jr. Lexington KY (12)

Dr. Jeffrey Rosen Coral Gables FL (36), Dr. Eli Roth Cincinnati OH (28)

Dr. John Rubino Raleigh NC (21), Dr. Steven Russell Philadelphia PA (5)

Dr. Robert Schreiman Santa Ana CA (39), Dr. Sherwyn Schwartz San Antonio TX (23), Dr. William Seger Fort Worth TX (23), Dr. Danny Sugimoto Chicago IL (90), Dr. Allen Sussman Renton WA (33), Dr. Phillip Toth Indianapolis IN (61)

Dr. Sunil Verma Warwick RI (25), Dr. Aaron Vinik Norfolk VA (8), Dr. Ralph Wade Bountiful UT (14)

II. Key Study Personnel

Study Oversight

Randomization was conducted using a telephone-based system with fax-back confirmation. Subjects were randomly allocated using a 5 digit subject number by study center with blocks of 6 subject numbers per block (4 bromocriptine-QR and 2 placebo per block). All

study drug was bottled centrally with unique bottle numbers and distributed by the VA Clinical Research Pharmacy, Albuquerque, NM. First patient enrolled 23 August 2004 and last patient completed 25 January 2007.

An independent data safety and monitoring board (DSMB) met quarterly and reviewed unblinded data. An independent safety monitor and safety officer processed all serious adverse events. Overall study oversight was by a steering committee consisting of two academic principle study investigators (Drs. Scranton and Gaziano), members responsible for site management coordination (Clinical Research Management of Agawam, MA and Veterans Affairs Cooperative Studies Program center located in Boston, MA), and members of the data and statistical coordinating center (EVEREST Inc., Toronto, CA).

Safety Study

Name	Affiliation/Contact Information
Dean Rutty, MSc Study Biostatistician	Everest Clinical Research Services, Inc 675 Cochrane Drive, Suite 408, East Tower Markham, Ontario, Canada L3R 0B8

Data Safety Monitoring Committee (DSMC)

Name	Affiliation/Contact Information
Jonathan Seltzer, MD, MBA, MA, FACC Cardiologist: DSMC Chair	Applied Clinical Intelligence, LLC 212C Race Street Philadelphia, PA 19106
Timothy Allan Shapiro, MD Cardiologist	380 Lankenau Medical Science Building 100 Lancaster Avenue West of City Line Wynnewood, PA 19096
Jerry Gardener, MD Endocrinologist	Science for Organizations, Inc. 156 Terrace Drive Chatham, NJ 07928
Lawrence Leiter, MD Endocrinologist	Head, Division of Endocrinology & Metabolism St. Michael's Hospital 6121Q-61 Queen Street East Toronto, Ontario M5C 2T2
Irving Hwang, PhD Biostatistician	Irving Consulting Group P. O. Box 258 Pluckemin, New Jersey 07978-0258
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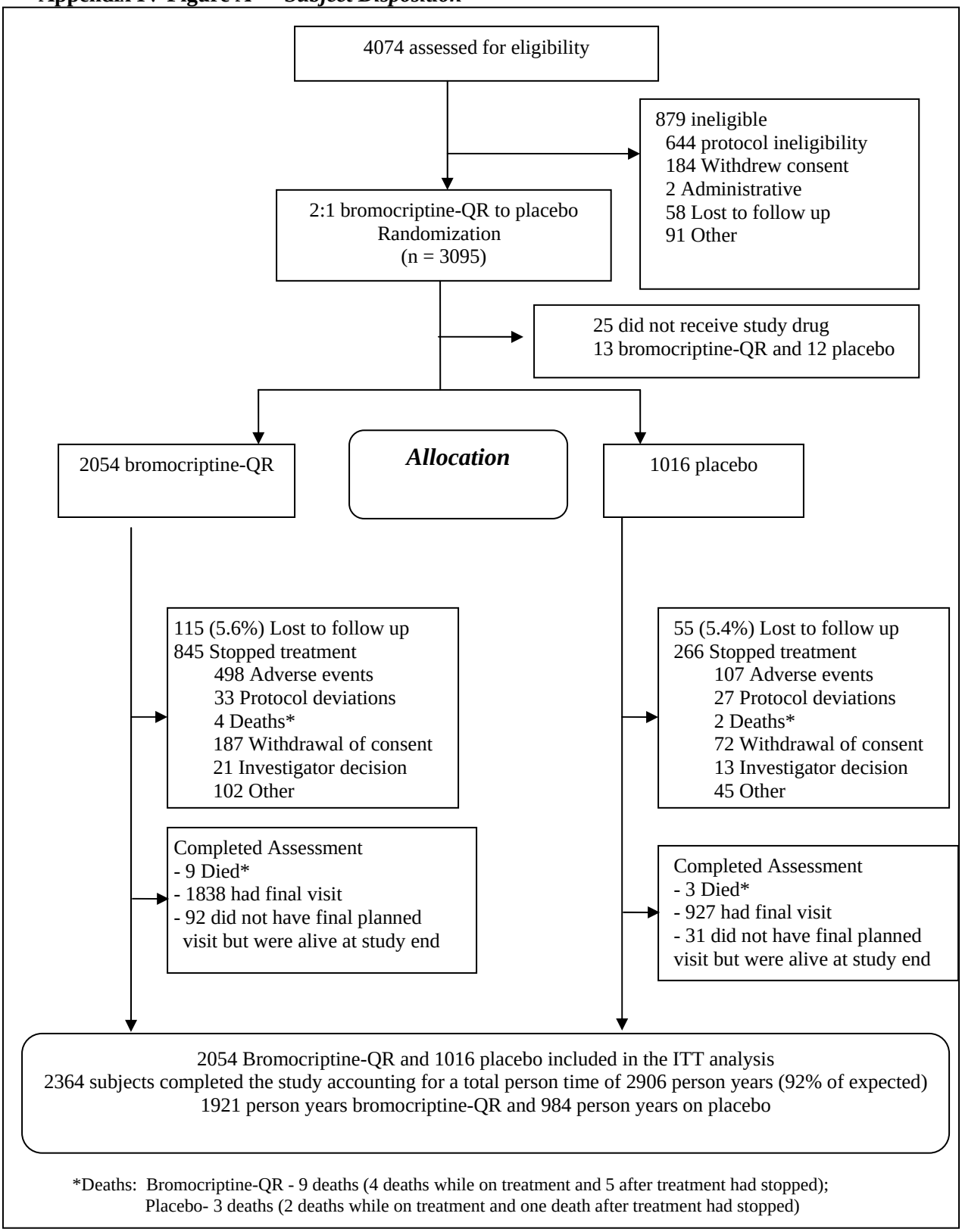
Event Adjudication Committee Members

Name/Role	Affiliation/Contact Information
Christopher O'Connor MD, FACP, FACC EAC Chair	Professor of Medicine Duke Clinical Research Institute
Peter Carson MD	Washington D.C. VA Medical Center
Jennifer Green, MD	Duke University Medical Center Division of Endocrinology, Metabolism, and Nutrition

III. Disclosures

Dr. Gaziano reports that he currently or in the past two years has received investigator-initiated federal funding from National Institutes of Health (NCI, NHLBI, NIA, NEI) and the VA (CSP) and non-federal investigator initiated funding from Amgen and Pliva; has received research support in the form of pills and or packaging from Wyeth Pharmaceuticals; has received honoraria from Bayer and McNeil Consumer Products for speaking engagements. Dr. Scranton has served within in the past five years as consultant or advisor for Berlex, Sanofi-Aventis; a scientific investigator for Pfizer Inc, MERCK, Pliva, Berlex Pharmaceuticals, and received research funding from Pharmerit North America and VA (CSP), and currently serves as the Chief Medical Officer for VeroScience. Anthony Cincotta is the Chief Science Officer of VeroScience. Dean Rutty and Jonathon Ma report no conflicts of interest.

Appendix IV Figure A — *Subject Disposition*



*Deaths: Bromocriptine-QR - 9 deaths (4 deaths while on treatment and 5 after treatment had stopped);
Placebo- 3 deaths (2 deaths while on treatment and one death after treatment had stopped)

Appendix IV Table B — *Baseline and change from baseline laboratory and blood pressure data in patients with Type 2 Diabetes*

	Level at Baseline		Change from Baseline		
	Bromocriptine-QR	**Placebo**	**Bromocriptine-QR**	**Placebo**	**p value**
	%		Absolute change		
HbA1c, median (IQR)	6.7 (6.2 , 7.5)	6.8 (6.2, 7.6)	0.1 (-0.3, 0.5)	0.2 (-0.3, 0.7)	0.0002
Lipids	mmol/l		% change		
Triglycerides, median (IQR)	1.6 (1.1, 2.4)	1.67 (1.2, 2.4)	-5 (-26.0, 23.2)	-0.4 (-22.7, 23.6)	0.0283
LDL cholesterol, median (IQR)	2.4 (1.9, 2.9)	2.36 (1.9 - 2.9)	-1.6 (-17.0, 15.6)	-1.2 (-16, 16.0)	0.6312
HDL cholesterol, median (IQR)	1.1 (1.0, 1.3)	1.1 (0.9, 1.3)	-2.5 (-10.5, 6.4)	-3.2 (-10.7, 5.9)	0.1807
Total cholesterol, median (IQR)	4.4 (3.8, 5.0)	4.3 (3.8, 5.0)	-2.1 (-11.9, 8.9)	-1.5 (-11.6, 9.6)	0.4784
	Ratio		% change		
Total cholesterol/HDL ratio, median (IQR)	3.85 (3.2, 4.6)	3.8 (3.3, 4.5)	0.44 (- 10.4, 12.2)	1.8 (-8.6, 13.8)	0.1211
	mm Hg		Absolute change		
Blood pressure:[†]					
Systolic blood pressure, median (IQR)	130 (120, 140)	130 (120, 139)	-2.0 (-13.0, 8.0)	0.0 (-10.0, 10.0)	0.0182
Diastolic blood pressure, median (IQR)	78 (70, 82)	77 (70, 82)	-2.0 (-9.0, 5.0)	-1.0 (-8.0, 5.0)	0.0249

[†]blood pressure value at screening visit

p-value comparing the two treatment arms is calculated using Wilcoxon Rank Sum test

Hb = hemoglobin,; HDL = high density lipoprotein, LDL = low density lipoprotein; IQR interquartile range

Appendix V Consort Statement

PAPER SECTION And topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned").	1
INTRODUCTION Background	2	Scientific background and explanation of rationale.	1
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	1-2
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	2-3
Objectives	5	Specific objectives and hypotheses.	3-4
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	4
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	4-5
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Appendix II
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	Appendix II
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Appendix II
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	Appendix II
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	5
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	5 appendix IV
Recruitment	14	Dates defining the periods of recruitment and follow-up.	Appendix II
Baseline data	15	Baseline demographic and clinical characteristics of each group.	6, Table 1
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	5
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	7, table 2
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	3-4; 6-7
Adverse events	19	All important adverse events or side effects in each intervention group.	7-9
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	9-11
Generalizability	21	Generalizability (external validity) of the trial findings.	10
Overall evidence	22	General interpretation of the results in the context of current evidence.	11