PEGASUS-TIMI (2010-2015) A phase 3 randomized, double-blind, placebo controlled, parallel group, multinational trial, to assess the prevention of thrombotic events with ticagrelor compared to placebo on a background of acetyl salicylic acid (ASA) therapy in patients with history of myocardial infarction. Primary outcome measures was any event after randomization from the composite of cardiovascular death, non-fatal MI, or non-fatal stroke. Industry sponsored.

COSMIC-HF Trial (2013-2015) A phase 2 double-blind, randomized, placebo-controlled, multicenter, dose escalation study to select and evaluate an oral modified release formulation of omecamtiv mecarbil in subjects with HF and left ventricular systolic dysfunction. The primary objectives of this study was (i) to select an oral modified release (MR) formulation and dose of omecamtiv mecarbil for chronic twice daily (BID) dosing in subjects with HF and left ventricular systolic dysfunction and (ii) to characterize its pharmacokinetics (PK) after 12 weeks of treatment. Industry sponsored.

LMS 002 (2011-2014) A phase 3 multicenter, double-blind, placebo-controlled randomized discontinuation study followed by an open-label extension period to evaluate the efficacy and safety of amifampridine phosphate (3,4-diaminopyridine phosphate) in patients with Lambert-Eaton Myasthenic Syndrome (LEMS). Primary outcome measure was change from baseline Quantitative Myasthenia Gravis (QMG) at 14 days. Industry sponsored.

Lurasidone HCl (2008-2014) Select trials in a phase 3 clinical development will include multiple independent trials of SM-13496. One trial is randomized, placebo and-active comparator controlled, clinical trial to study the safety and efficacy of two doses of lurasidone HCI in acutely psychotic patients with schizophrenia. The primary outcome measure was change in total PANSS score from baseline to the end of the double blind treatment period.

ATOMIC-AHF (2011-2013) A phase 2, double blind, placebo controlled, multicenter study to evaluate the safety and efficacy of IV infusion treatment with omecamtiv mecarbil in subject with left ventricular systolic dysfunction hospitalized for acute heart failure. The primary objective of the study is to evaluate the effect of 48 hours of intravenous (IV) omecamtvi mecarbil compared with placebo on dyspnea in subjects with left ventricular systolic dysfunction hospitalized for acute heart failure. Industry sponsored.

LPL100601 and SB-480848/033 (2008-2013) The Phase III Program includes: A Clinical Outcomes Study Of Darapladib Versus Placebo In Subjects With Chronic Coronary Heart Disease (CHD) To Compare The Incidence Of Major Adverse Cardiovascular Events (LPL100601) **AND**, A Clinical Outcomes Study of Darapladib Versus Placebo In Subjects With Acute Coronary Syndrome (ACS) To Compare The Incidence of Major Adverse Cardiovascular Events (MACE) (SB-480848/033). Industry sponsored.

White HD, Held C, Stewart R, et al; STABILITY Investigators. Darapladib for preventing ischemic events in stable coronary heart disease. *The New England Journal of Medicine* 370(18): 1702-0711, 2014.

O'Donaghue ML, Braunwald E, White HD, Steen DL, et al; SOLID-TIMI 52 Investigators. Effect of darapladib on major coronary events after an acute coronary syndrome. The

SOLID-TIMI 52 Randomized Clinical Trial. *Journal of the American Medical Association* 312(10): 1006-1015, 2014.

REDHF Trial (2006 -2013) A phase 3, double blind, randomized, placebo controlled, multicenter study to assess the efficacy and safety of darbepoetin alfa treatment on mortality and morbidity in heart failure (HF) subjects with symptomatic left ventricular systolic dysfunction and anemia. Primary endpoint was time to death from any cause or first hospital admission for worsening HF, whichever occurred first. Industry sponsored

Swedberg K, Young JB, Anand IS, Cheng S, Desai AS, Diaz R, Maggionia AP, McMurray JJV, O'Connor C, Pfeffer MA, Solomon SD, Sun Y, Tnedera M, van Veldhuisen DJ, for the RED-HF Committees and Investigators. Treatment of anemia with darbepoetin alfa in systolic heart failure. *The New England Journal of Medicine* 368(13): 1210-19, 2013.

AMG 785 (2009-2012) A phase 2 clinical trial studied the safety and efficacy of AMG 785, an investigational bone building agent, in the treatment of postmenopausal women with low bone mineral density. Different doses and dosing frequencies of AMG 785 were compared to placebo in a double-blind fashion. The primary outcome was percent change from baseline in lumbar spine bone mineral density. Industry sponsored.

McClung MR, Grauer A, Boonen S, Bolobnese MA, Brown JP, Diez-Perez A, Langdahl BL, Reginster J-Y, Zanchetta JR, Wasserman SM, Katz L, Maddox J, Yang Y-C, Libanati C, Bone HG. Romosozumab in postmenopausal women with low bone mineral density. *The New England Journal of Medicine* 370 (5):412-20, 2014.

A8851009 (2007-2011) A phase 3 prospecitive, randomized trial comparing the efficacy of anidulafungin and voriconazole in combination to that of voriconazole alone when used for primary therapy of proven or probable invasive aspergillosis (IA). The primary endpoint was all cause mortality, measured 6 weeks after IA initiation of study drug in subjects with proven or probable IA.

Marr KA, Schlamm H, Rottinghaus ST et.al. A randomised, double-blind study of combination antifungal therapy with voriconazole and anidulafungin versus voriconazole monotherapy for primary treatment of invasive aspergillosis. In: Abstracts of the Twenty-second European Congress of Clinical Microbiology and Infectious Diseases, London, UK, 2012: Abstract LB 2812. European Society of Clinical Microbiology and Infectious Diseases, Basel, Switzerland.

MGA031 (2006- 2011) A phase 2/3, randomized, double blind, multicenter, multinational, 4-arm, controlled, dose ranging study to evaluate efficacy and safety of MGA031, a humanized, FcR non-binding, anti-CD3 monoclonal antibody, in children and adults with recent-onset type 1 diabetes mellitus. Industry sponsored.

Sherry N, Hagopian W, Ludvigsson J, Jain SM, Wahlen J, Ferry Jr RJ, Bode B, Aronoff S, Holland C, Carlin D, King KL, Wilder RL, Pillemer S, Bonvini E, Johnson S, Stein KE, Koenig S, Herold KC, Daifotis AG, for the Protégé Trial Investigators. Teplizumab for treatment of type 1 diabetes (Protégé study):1-year results from a randomised, placebo-controlled trial. *Lancet* DOI:10.1016/S0140-6736(11)60931-8, 2011.

TREAT (2004-2010) A randomized, double blind, multicenter study to assess the effect of anemia therapy with darbepoetin alpha on the composite event comprising all cause mortality and cardiovascular (CV) events in subjects with both chronic kidney disease (CKD) and Type 2 diabetes mellitus (DM). Industry sponsored.

> Mix TH, Brenner RM, Cooper ME, de Zeeuw D, Ivanovich P, Levey AS, McGill JB, McMurray JJ, Parfrey PS, Parving H-H, Pereira BJ, Remuzzi G, Singh AK, Solomon SD, Stehman-Breen C, Toto RD, Pfeffer MA. Rationale-Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT): Evolving the management of cardiovascular risk in patients with chronic kidney disease. *American Heart Journal* 149 (3):408-13, 2005.
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> Pfeffer MA, Burdmann EA, Chen C-Y, Cooper ME, de Zeeuw D, Eckardt K-U, Feyzi JM, Ivanovich P, Kewalramani R, Levey AS, Lewis EF, McGill JB, McMurray JJ, Parfrey P, Parving H-H, Remuzzi G, Singh AK, Solomon SD, Toto R, for the TREAT Investigators. A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease. *New England Journal of Medicine* 361(21):2019-32, 2009.

PLATO (2006-2009) A randomized, double blind, parallel group, international, multicenter study comparing the efficacy and safety of AZD6140 90mg twice daily with clopidogrel 75mg once daily in the prevention of fatal and nonfatal cardiovascular events in patients with non-ST or ST elevation ACS. Industry sponsored.

> Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA, for the PLATO Investigators. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *New England Journal of Medicine* 361(11):1045-57, 2009.

CP-945,598 Obesity (2007-2009) A phase 3 clinical development program to evaluate the efficacy and safety of CP-945,598 in the treatment of obese subjects. The program was terminated on November 3, 2008 due to changing regulatory perspectives on the risk/benefit profile of the drug class and likely new regulatory requirements for approval. No safety issues were involved in the termination decision. Industry sponsored.

RWJ333369 (2006-2008) A randomized, double blind, placebo controlled, dose-titration study to determine safety, tolerability and preliminary efficacy of RWJ-333369 as adjunctive therapy in subjects with treatment-resistant partial seizures or primarily generalized tonic-clonic seizures. Industry sponsored.

> Sperling MR, Greenspan A, Cramer JA, Kwan P, Kälviäinen R, Halford JJ, Schmitt J, Yuen E, Cook T, Haas M, Novak, G. Carisbamate as adjunctive treatment of partial onset seizures in adults in two randomized, placebo-controlled trials. *Epilepsia* 51(3): 333-343, 2010.

I-PRESERVE (2002-2008) A randomized, double blind, multicenter study comparing Irbesartan, an angiotensin II receptor antagonist, verus placebo in subjects with advanced heart failure and with preserved systolic function. Primary endpoint is all cause mortality or cardiovascular morbidity. Industry sponsored.

> Massie B, Carson PE, McMurray JJ, Komajda M, McKelvie R, Zile MR, Anderson S, Donovan M, Iverson E, Staiger C, Praszynska A, I-PRESERVE Investigators. Irbesartan

in patients with heart failure and preserved ejection fraction. *The New England Journal of Medicine* 359 (23):2456-67, 2008.

CORONA (2004-2007) A phase 3, randomized, double blind, placebo controlled study with rosuvastatin in subjects with chronic symptomatic systolic heart failure. Comparison of rosuvastatin, along with all other medications prescribed, versus placebo. Combined primary endpoint was cardiovascular death or non-fatal MI or non-fatal stroke. Industry sponsored. Results presented at the November 2007 American Heart Association meeting.

Kjekshus J, Apetrei E, Barrios V, Böhm M, Cleland JGF, Cornel JH, Dunselman P, et al; for the CORONA Group. Rosuvastatin in older patients with systolic heart failure. New England Journal of Medicine 357(22):2248-61, 2007.

COX 2 INHIBITOR PROGRAM (2005-2007) This clinical development program for a dual-acting COX2 inhibitor was expected to include approximately 40,000 subjects in 36 phase 3 multicenter, randomized, placebo-and active comparator-controlled, studies in multiple indications including osteoarthritis, rheumatoid arthritis, chronic low back pain, neuropathic pain, visceral pain and acute pain. The program was terminated early due to insufficient efficacy in initial studies. Industry sponsored.

EVEREST (2003-2007) A randomized, multicenter, double blind study comparing tolvaptan, a vasopressin receptor antagonist, in conjunction with optimal current therapy on the time to all-cause mortality, versus placebo in subjects with worsening congestive heart failrue. Primary outcomes are all cause mortality, cardiovascular mortality or CHF morbidity and global clinical status. Industry sponsored.

Konstam MA, Gheorghiade M, Burnett JC Jr., Grinfeld L, Maggioni AP, Swedberg K, Udelson JE, Zannad F, Cook T, Ouyang J, Zimmer C, Orlandi C. Effects of oral tolvaptan in patients hospitalized for worsening heart failure. *Journal of the American Medical Association* 297(12): 1319-1331, 2007.

Gheorghiade M, Konstam MA, Burnett JC Jr., Grinfeld L, Maggioni AP, Swedberg K, Udelson JE, Zannad F, Cook T, Ouyang J, Zimmer C, Orlandi C. Short-term clinical effects of tolvaptan, an oral vasopressin antagonist, in patients hospitalized for heart failure. *Journal of the American Medical Association* 297(12): 1331-1343, 2007.

ARIES (2004-2006) Two phase 3, randomized, double blind, placebo controlled, multicenter, efficacy studies of ambrisentan in subjects with pulmonary arterial hypertension. Primary endpoint was the change from baseline in the six-minute walk distance evaluated after 12 weeks of therapy. Industry sponsored.

Galié N, Olschewski H, Oudiz RJ, Torees F, Frost A, Ghofrani HA, Badesch DB, McGoon MD, McLaughlin VV, Roecker EB, Gerber MJ, Dufton C, Wiens BL, Rubin LJ, and for the Ambrisentanin Pulmonary Aterial Hypertension, Randomized, Double-Blind, Placebo-Controlled, Multicenter, Efficacy Studies (ARIES) Group. Amberisentan for the treatment of pulmonary arterial hypertension: Results of the Ambrisentanin Pulmonary Aterial Hypertension, Randomized, Double-Blind, Placebo-Controlled, Multicenter, Efficacy (ARIES) Study 1 and 2. *Circulation* 117:3010-3019, 2008.

ILLUMINATE (2004-2006) A multi-center, double blind, randomized, parallel group evaluation of the fixed combination torcetrapib/atorvastatin, administered orally, once daily, compared with

atorvastatin alone, on the occurrence of major cardiovascular events in subjects with coronary heart disease or risk equivalents. Industry sponsored. Results presented at the November 2007 American Heart Association meeting.

> Barter PJ, Caulfield M, Eriksson M, Grundy SM, Kastelein JP, Komajda M, Lopez-Sendon J, Mosca L, Tardif J, Waters DD, Shear Cl, Revkin JH, Buhr KA, Fisher MR, Tall AR, Brewer B, for the ILLUMINATE Investigators. Effects of torcetrapib in patients at high risk for coronary events. *The New England Journal of Medicine* 357 (21):2109-22, 2007.

PAD20001 (2004 -2006) A multicenter, two staged, parallel, randomized, double blind, placebo controlled study of the safety, tolerability and effects on plasma high density lipoprotein cholesterol of 12 weeks treatment with daily doses in subjects with low HDLc. Industry sponsored.

ADOPT (2000-2006) A randomized, double blind clinical trial to compare the durability of glucose lowering and preservation of pancreatic beta cell function of rosiglitazone monotherapy compared to metformin or glyburide/glibenclamide in subjects with drug-naïve, recently diagnosed Type 2 diabetes mellitus. Primary outcome was monotherapy failure. Industry sponsored.

> Kahn, SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, Kravitz BG, Lachin JM, O'Neill C, Zinman B, Viberti G for the ADOPT Study Group. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. *New England Journal of Medicine* 355(23):2427-53, 2006.

CSMS 802 & 804 (1999-2006) A randomized, double blind study on the efficacy and safety of Sandostatin LAR in the therapy of subjects with moderately severe or severe non-proliferative diabetic retinopathy (NPDR) or low risk proliferative diabetic retinopathy (PDR). Primary outcome was progression of retinopathy. Industry sponsored.

PAA20001 (2004-2005) A multicenter, three staged, randomized, parallel group, double blind, fenofibrate and placebo controlled dose-response evaluation of the safety, tolerability and effects on plasma high-density lipoprotein cholesterol and triglycerides of eight weeks treatment with daily doses in otherwise healthy subjects with low HDLc, mildly to moderately elevated triglycerides and normal low-density lipoprotein cholesterol. Study drug was a peroxisome proliferator-activated receptor (alpha) agonist. Industry sponsored.

DISPERSE2 (2004-2005) A double blind, double-dummy, parallel group randomized dose confirmation and feasibility study of AZD6140 + Acetyl Salicylic Acid (ASA) compared with clopidogrel + ASA in patients with non-ST segment elevation acute coronary syndromes. Industry sponsored.

AGT (2003-2005) A randomized, double blind, placebo controlled clinical trial to evaluate the efficacy and safety of Ad5FGF. Primary outcome was change from baseline in treadmill exercise duration at 12 weeks following treatment. Industry sponsored.

APC (2001-2005) A randomized, double blind, multicenter, placebo controlled study to evaluate the efficacy and safety of celecoxib in reducing the percentage of adenoma subjects with newly detected adenomas at surveillance colonoscopy. Comparison of two doses of celecoxib, a COX-2 inhibitor, versus placebo. Primary outcome was the occurence of new adenomatous

polyps. NCI and industry sponsored. Results presented at April 2006 American Association for Cancer Research Annual Meeting.

> Bertagnolli MM, Eagle CJ, Zauber AG, Redston M, Solomon SD, Kim K, Tang J, Rosenstein RB, Wittes J, Corle D, Hess TM, Woloj GM, Boisserie F, Anderson, WF, Viner JL, Bagheri D, Burn J, Chung DC, Dewar T, Foley TR, Hoffman N, Macrae F, Pruitt RE, Saltzman JR, Salzberg B, Sylwestrowicz T, Gordon GB, Hawk ET for the APC Study Investigators. Celecoxib for the prevention of sporadic colorectal adenomas. *New England Journal of Medicine* 355(9):873-84, 2006.

VERITAS (2003-2004) A randomized, multicenter, double blind, placebo controlled, parallel group study to assess the efficacy, safety, and tolerability of tezosentan in subjects with acute heart failure. Primary endpoint was the incidence of death or worsening heart failure at 7 days following study drug initiation. Industry sponsored.

ESSENTIAL (2001-2004) A phase 3, randomized, double blind, multicenter, parallel group, placebo controlled study of oral enoximone versus placebo in adbanced chronic heart failure subjects. Primary outcome was all cause mortality or cardiovascular hospitalization. Industry sponsored.

> Metra M, Eichhorn E, Abraham WT, Linseman J, Böhm M, Corbalan R, DeMets D, DeMarco T, Elkayam U, Gerber M, Komajda M, Liu P, Mareev V, Perrone SV, Poole-Wilson P, Roecker E, Stewart J, Swedberg K, Tendera M, Wiens B, Bristow MR for the ESSENTIAL Investigators. Effects of low-dose oral enoximone administration on mortality, morbidity, and exercise capacity in patients with advanced heart failure: the randomized, double-blind, placebo-controlled, parallel group ESSENTIAL trials. *European Heart Journal* 30:3015-26, 2009.

TNT (2000-2004) A randomized, double blind, parallel group study of the effect of LDL-Cholesterol lowering beyond currently recommended minimum targets on coronary heart disease (CHD) recurrence in subjects with pre-existing CHD. Primary outcome was major CHD event defined as either CHD death or non-fatal myocardial infarction. Industry sponsored, Results presented at March 2005 American College of Cardiology Late-Breaking Trials.

> LaRosa, JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, Gotto AM, Greten H, Kastelein JJ, Shepherd J, Wenger NK for the Treating to New Targets Investigators. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *The New England Journal of Medicine* 352:1425-35, 2005.

SPORTIF 3 and V (2000-2004) A randomized, multicenter, multinational, double blind, parallel group study in subjects with chronic non-valvular atrial fibrillation. Primary outcome was stroke and systemic embolic events. Industry sponsored. Results from SPORTIF 3 were presented at April 2003 American College of Cardiology Late-Breaking Trials.

> Executive Steering Committee on behalf of the SPORTIF 3 Investigators. Stroke prevention with the oral direct thrombin inhibitor ximelagatran compared with warfarin in patients with non-valvular atrial fibrillation (SPORTIF 3): randomized controlled trial. *The Lancet* 362: 1691-98, 2003.

Executive Steering Committee for the SPORTIF 5 Investigators. Ximelagatran vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation; a randomized trial. *Journal of the American Medical Association* 293:690-98, 2005.

DFMO in Bladder Cancer (1999-2004) A phase 3, randomized, multicenter double blind chemoprevention clinical trial comparing DFMO versus placebo in subjects with low-grade superficial bladder cancers. Primary outcome was disease recurrence. Jointly sponsored by NCI and industry.

DFMO in Skin Cancer (1998-2004) A phase 3, randomized double blind, placebo controlled skin cancer prevention study of DFMO in subjects with previous history of skin cancer. Primary outcome was rate of new skin cancer development. NCI sponsored.

COMPANION (1999-2002) An open-label, prospective, multicenter, randomized clinical trial. Comparison of optimal drug treatment versus optimal drug treatment with biventricular pacing versus optimal drug treatment with biventricular pacing and defibrillation. Primary endpoint was all-cause mortality/all-cause hospitalization. Results presented at March 2003 American College of Cardiology Late-Breaking Trials and September 2003 Heart Failure Society of America Late-Breaking Trials.

Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, DiCarlo L, DeMets D, White BG, DeVries DW, and Feldman AM. Cardiac-Resynchronization Therapy with or without and Implantable Defibrillator in Advanced Chronic Heart Failure. *The New England Journal of Medicine* 350: 2140-50, 2004.

Carson P, Anand I, O'Connor C, Jaski B, Steinber J, Lwin A, Lindenfeld J. Ghali J, Barnet J, Feldman AM, Bristow MR. Mode of Death in Advanced Heart Failure: the Comparison of Medical, Pacing, and Defibrillation Therapies in Heart Failure, *Journal of the American College of Cardiology* 46, No. 12: 2329-34, 2005.

ENABLE (1999-2001) A randomized, double blind, placebo controlled study to assess the effects of Ro 47-0203 (Bosentan) on the morbidity and mortality of subjects with chronic heart failure. Primary endpoints were (1) all-cause mortality/hospitalization for heart failure and (2) clinical status at nine months. Industry sponsored. Results presented at March 2002 American College of Cardiology Late-Breaking Trials.

WIZARD (1997-2001) A phase 3, randomized, double blind, placebo controlled trial of the effect of weekly azithromycin on the incidence of coronary artery disease in subjects with evidence of exposure to C. Pneumoniae. Primary outcome was progression of clinical coronary artery disease. Industry sponsored. Results presented at March 2002 American College of Cardiology Late-Breaking Trials.

O'Connor CM, Dunne MW, Pfeffer MA, Muhlestein JB, Yao L, Gupta S, Benner RJ, Fisher MR, Cook TD. Azithromycin for the secondary prevention of coronary hearth disease events. *Journal of the American Medical Association* 290:1459-1466, 2003.

Aguilar D, Fisher MR, O'Connor CM, Dunne MW, Muhlestein JB, Yao L, Gupta S, Benner RJ, Cook TD, Edwards D, Pfeffer MA. Metabolic syndrome, C-reactive protein, and prognosis in patients with established coronary artery disease. *American Heart Journal* 152(2):298-304, 2006.

VIETNAM TAMOXIFEN STUDY (1993-2001) A randomized clinical trial of adjuvant oophorectoy and tamoxifen in premenopausal women subjects with operable breast cancer from Vietnam and China. Primary outcomes were overall survival and recurrence free survival. Supported by grants from the US NIH CA 64339, University of Wisconsin Clinical Cancer Center, and by the International Breast Cancer Research foundation, Madison, Wisconsin, USA.

Love RR, Duc NB, Allred DC, Binh NC, Dinh NV, Kha NN, Thuan TV, Mohsin SK, Roanh leD, Khang HX, Tran TL, Quy TT, Thuy NV, The PN, Cau TT, Tung ND, Huong DT, Quang leM, Hien NN, Thuong L, Shen TZ, Xin Y, Xhang Q, Havighurst TC, Yang YF, Hillner BE, DeMets, DL. Oophorectomy and tamoxifen adjuvant therapy in premenopausal Vietnamese and Chinese women with operable breast cancer. *Journal of Clinical Oncology* 20:2559-2566, 2002.

Love RR, Nguyen BD, Havighurst TC, Mohsin SK, Zhang Q, DeMets DL, Allred DC. HER-2/neu Overexpression and Response to Oophorectomy Plus Tamoxifen Adjuvant Therapy in Estrogen Receptor-Positive Premenopausal Women with Operable Breast Cancer. *Journal of Clinical Oncology* 21:453-457, 2003.

COPERNICUS (1997-2000) A randomized, double blind, placebo controlled, multicenter, multinational clinical trial designed to determine the effect of carvedilol on all-cause mortality in subjects with severe chronic heart failure. A multinational study conducted in North and South America, Europe, Australia, and Asia. Primary endpoint was all-cause mortality. Industry sponsored. Results presented at August 2000 European College of Cardiology Meeting, November 2000 American Heart Association Meeting, and March 2001 American College of Cardiology Meeting.

Rouleau, J.L., Roecker, E.B., Tendera, M., Mohacsi, P., Krum, H., Katus, H.A., Fowler, M.B., Coats, A.J.S. and Packer, M. Influence of pretreatment systolic blood pressure on the effects of carvedilol in patients with severe chronic heart failure: The COPERNICUS study, *Journal of the American College of Cardiology* 43:1423-1429, 2004.

Krum, H., Mohacsi, P., Katus, H.A., Tendera, M., Rouleau, J.L., Fowler, M.B., Coats, A.J., Roecker, E.B. and Packer, M. Are beta-blockers needed in patients receiving spironolactone for severe chronic heart failure? An analysis of the COPERNICUS study, *American Heart Journal*, 151: 55-61, 2006.

Packer M, Coats A, Fowler M, Katus H, Krum H, Mohacsi P, Rouleau J, Tendera M, Castaigne A, Roecker E, Schultz M, and DeMets D, for the Carvedilol Prospective Randomized Cumulative Survival Study Group. Effect of Carvedilol on Survival in Severe Chronic Heart Failure. *New England Journal of Medicine* 344:1651-1658, 2001.

Packer M, Fowler MB, Roecker EB, Coats AJS, Katus HA, Krum H, Mohacsi P, Rouleau JL, Tendera M, Staiger C, Holcslaw TL, Amann-Zalan I, DeMets DL: Effect of carvedilol on the morbidity of patients with severe chronic heart failure. *Circulation* 106:2194-2199, 2002.

Krum H, Roecker EB, Mohacsi P, Rouleau JL, Tendera M, Coats AJS, Katus HA, Fowler MB, Packer M: Effects of initiating carvedilol in patients with severe chronic heart failure. *Journal of the American Medical Association* 289:712-718, 2003.

PRAISE 2 (1996-2000) A randomized, double blind study comparing Amlodipine, a calcium channel blocker, to placebo. Primary outcomes were all-cause mortality, cardiovascular mortality, and health care resource utilization. Industry sponsored. Results presented at March 2000 American College of Cardiology Meeting.

EXCITE (1997-1999) A randomized, double blind, parallel design, placebo controlled, international, multicenter study designed to compare the efficacy and safety of xemilofiban to placebo when administered to subjects prior to and for up to six months after percutaneous revascularization procedures. Primary outcome was occurrence of death, MI, or urgent revascularization at 6 months. Industry sponsored. Results presented at March 1999 American College of Cardiology Meeting.

O'Neil W, Serruys P, Knudtson M, van Es G, van der Zwaan C, Kleiman J, Gong J, Roecker E, Dreiling R, Alexander J, Anders R, for the EXCITE Trial Investigators. A Prospective Randomized Double-Blind Clinical Trial of Long-Term Oral Platelet Glycoprotein Receptor Blockade After Percutaneous Coronary Intervention. *New England Journal of Medicine* (342):1316-24, 2000.

MERIT (1997-1999) A randomized double blind, placebo controlled survival study with metoprolol CR/XL in subjects with decreased ejection fraction and symptoms of heart failure. Primary outcome was mortality with composite of all-cause mortality and all-cause hospitalization as a secondary endpoint. Industry sponsored. Results presented at March 1999 American College of Cardiology Meeting and at August 1999 European College of Cardiology Meeting.

MERIT-HF Study Group. Effect of Metoprolol CR/XL in Chronic Heart Failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure. *Lancet* 353:2001-2007, 1999.

Hjalmarson A, Goldstein S, Fagerberg B, et al, for the MERIT-HF Study Group. Effects of Controlled-Release Metoprolol on Total Mortality, Hospitalizations, and Well-being in Patient with Heart Failure, The Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). *Journal of the American Medical Association* 10:1295-1336, 2000.

REACH (1997-1998) A double blind, randomized, placebo controlled study to assess the effects of Ro 470203 (Bosentan) on the morbidity and mortality of subjects with chronic heart failure. Primary endpoint was change in clinical status. Industry sponsored. Results presented at 1998 American Heart Association Meeting.

THS 95.1 (1997-1998) A multicenter, randomized, placebo controlled study to asses the efficacy of Diaspirin cross-linked Hemoglobin (DCLHB) in the treatment of severe traumatic hemorrhagic shock. Primary outcome was 28 day mortality. Industry sponsored with special IND approved. First study conducted under DHHS Waiver of Informed Consent Requirements in Certain Emergency Research.

Sloan EP, Koenigsberg M, Gens D, Cipolle M, Runge J, Mallory MN, Rodman G, for the DCLHb Traumatic Hemorrhagic Shock Study Group. Diaspirin Cross-Linked Hemoglobin (DCLHb) in the Treatment of Severe Traumatic Hemorrhagic Shock: A Randomized Controlled Efficacy Trial. *Journal of the American Medical Association* 282:1857-1864, 1999.

Lewis RJ, Berry DA, Cryer H, Fost N, Krome R, Washington GR, Houghton J, Blue JW, Bechhofer R, Cook T, and Fisher M. Monitoring a Clinical Trial Conducted Under the Food and Drug Administration Regulations Allowing a Waiver of Prospective Informed Consent: The Diaspirin Cross-Linked Hemoglobin Traumatic Hemorrhagic Shock Efficacy Trial. *Annals of Emergency Medicine* 38:397-404, 2001.

AB-02 (1995-1998) A randomized, double blind clinical trial comparing Adenosin, an additive to cardioplegic solutions, versus placebo in subjects with depressed ventricular function undergoing coronary artery bypass graft surgery. Primary outcome was the amount of 1) dopamine and 2) inotropic support used during the first seven postoperative days. Industry sponsored.

VEST (1994-1998) A randomized. double blind study comparing Vesnarinone, an ionotropic drug, versus placebo in subjects with severe left ventricular heart failure. Primary outcome was mortality and cardiovascular morbidity. Industry sponsored and coordinated through an academic network. Results presented at November 1996 American Heart Association Meeting and at March 1997 American College of Cardiology Meeting.

Cohn J, Goldstein S, Greenberg B, Lorell B, Bourge R, Jaski B, Gottlieb S, McGrew F, DeMets D, and White B, for the VESNARINONE Trial Investigators. A dose-dependent increase in mortality with vesnarinone among patients with severe heart failure. *New England Journal of Medicine* 339:1810-1816, 1998.

CARS (1993-1997) A randomized, double blind study comparing Coumadin, warfarin, in two fixed doses with aspirin versus aspirin alone after the occurrence of a myocardial infarction. Primary outcome was occurrence of clinical events. Industry sponsored. Results presented at March 1996 and March 1997 American College of Cardiology Meeting and at November 1997 American Heart Association Meeting.

Coumadin Aspirin Reinfarction Study (CARS) Investigators. Randomized Double-Blind Trial of Fixed Low Dose Warfarin with Aspirin After Myocardial Infarction. *Lancet* 350 (9075): 389-396, 1997.

ACTS (1992-1995) A randomized, double blind study comparing rHCNTF, a neurotrophic growth factor, in two doses versus placebo in subjects with amyotrophic lateral sclerosis. Primary outcome was rate of change from baseline in isometric muscle strength to nine months. Industry sponsored. SDAC served as the data management center as well as the analysis center. Results presented at May 1995 American Academy of Neurology Meeting.

ALS CNTF Treatment Study Group. A Double-Blind Placebo-Controlled Clinical Trial of Subcutaneous Recombinant Human Ciliary Neurotrophic Factor (rHCNTF) in Amyotrophic Lateral Sclerosis. *Neurology* 46:1244-1249, 1996.

PRAISE (1992-1994) A randomized, double blind study comparing Amlodipine, a calcium channel blocker, versus placebo in subjects with severe heart failure (Class 3b and 4). Primary outcomes were all-cause mortality and hospitalization for major cardiovascular events. Industry sponsored.

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