

## ROAD MAPS TO ACHIEVE GLYCEMIC CONTROL IN TYPE 2 DIABETES MELLITUS

### *ACE/AACE Diabetes Road Map Task Force*

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The accompanying Diabetes Road Maps were created to provide direction for clinicians in achieving the hemoglobin A1c (A1C) glycemic goals established by the American College of Endocrinology (ACE) and the American Association of Clinical Endocrinologists (AACE). The three Road Maps consist of the following: one for treatment-naïve patients (Fig. 1), one for treated patients not at A1C goal (Fig. 2), and a third focusing on the prevention of diabetes (Fig. 3). The Road Maps feature individualized treatment regimens based on the presenting A1C in treatment-naïve patients or the current A1C in treated patients, and they stress the need to advance therapy if the A1C goal is not met within 3 months. The importance of targeting the treatment of postprandial hyperglycemia in the lower A1C ranges is emphasized. The following should be noted:

1. The evidence base for each of the medications listed in the columns of the Road Maps can be found in the appended bibliography, and the listed resources are annotated with the levels of evidence. Recommendations are based on A1C-lowering data from US Food and Drug Administration (FDA)-approved clinical trials as well as from the large randomized placebo- or comparator-controlled clinical trials published in peer-reviewed journals, and they are consistent with FDA-approved indications.
2. The relative or rank order of the medications listed in the Road Maps is derived from valid comparator trial data that were available. Because of the paucity of such well-designed head-to-head studies, however, the order of medications is provided as a template, is considerably dictated by the preference of the authors, and is based on extensive clinical experience. Therefore, the recommended order of interventions can be categorized primarily as expert opinions of the Diabetes Road Map Task Force.

It is hoped that these Road Maps will be helpful to clinicians in outlining the therapeutic options currently available to achieve the optimal level for glycemic control, as proposed by ACE and AACE.

### DISCLOSURE

Dr. Lawrence Blonde has received grant and/or research support from Amylin Pharmaceuticals, Inc., AstraZeneca, Bristol-Myers Squibb Company, Eli Lilly and Company, MannKind Corporation, Merck & Co., Inc., Novartis Pharmaceuticals Corporation, Novo Nordisk Inc., Pfizer Inc., and sanofi-aventis. He has received speaker and consultant honoraria from Abbott Laboratories, Amylin Pharmaceuticals, Inc., GlaxoSmithKline, LifeScan, Inc., Eli Lilly and Company, Merck & Co., Inc., Novartis Pharmaceuticals Corporation, Novo Nordisk Inc., Pfizer Inc., and sanofi-aventis. He has received consultant honoraria from KOS Pharmaceuticals and U.S. Surgical Corporation. Dr. Blonde has also disclosed that his spouse is a stock shareholder of Amylin Pharmaceuticals, Inc. and Pfizer Inc., in an account that is not part of their community property.

Dr. Jaime A. Davidson has received consultant and/or speaker honoraria from Bristol-Myers Squibb Company, Calixto Medical, CureDM, Inc., Genex Biotechnology Corporation, GlaxoSmithKline, Johnson & Johnson, Eli Lilly and Company, Merck Germany, Merck Sharp & Dohme, Novartis Pharmaceuticals Corporation, Novo Nordisk Inc., Pfizer Inc., Roche Pharmaceuticals, sanofi-aventis, Stein Laboratories, and Takeda Pharmaceuticals America, Inc.

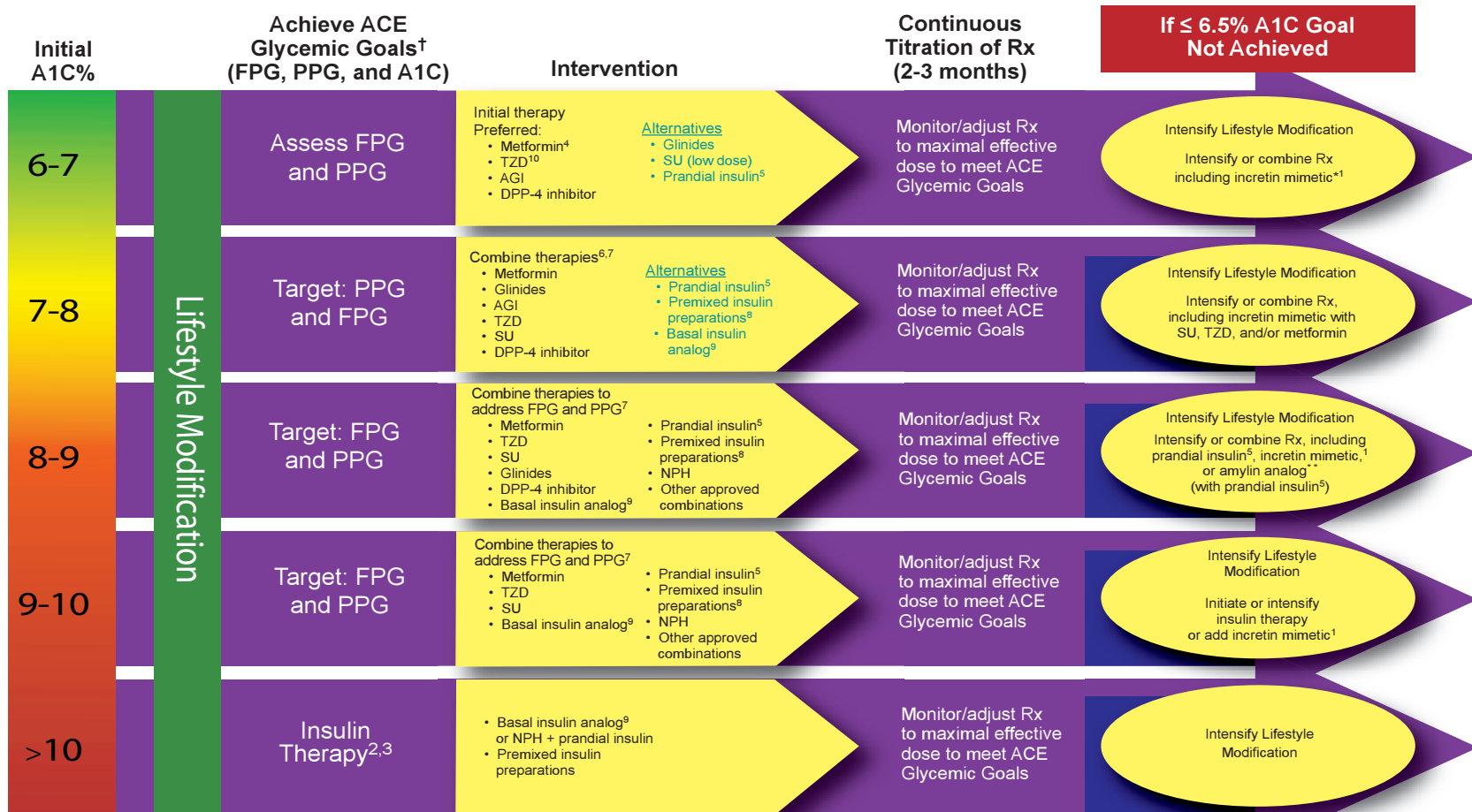
Dr. Daniel Einhorn has received clinical research support from Allergan, Inc., Eli Lilly and Company, Medtronic, Inc., Pfizer Inc., and sanofi-aventis. He has received consultant honoraria from Amylin Pharmaceuticals, Inc., Eli Lilly and Company, MannKind Corporation, Medtronic, Inc., and Takeda Pharmaceuticals America, Inc. He has received speaker honoraria from Amylin Pharmaceuticals, Inc., Merck & Co., Inc., sanofi-aventis, and Takeda Pharmaceuticals America, Inc.

Dr. George Grunberger has received grant/research support from Eli Lilly and Company, Mitsubishi, Pfizer Inc., and sanofi-aventis. He has received speaker honoraria from Amylin Pharmaceuticals, Inc., AstraZeneca, GlaxoSmithKline, Eli Lilly and Company, Merck & Co., Inc., Novo Nordisk Inc., Pfizer Inc., and sanofi-aventis.

## Road Map to Achieve Glycemic Goals: Naïve to Therapy (Type 2)

**Abbreviations in Road Maps:**

AAACE = American Association of Clinical Endocrinologists; A1C = hemoglobin A1c; ACE = American College of Endocrinology; AGI =  $\alpha$ -glucosidase inhibitor; DPP-4 = dipeptidyl peptidase-4; FDA = US Food and Drug Administration; FPG = fasting plasma glucose; HDL = high-density lipoprotein; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; MNT = medical nutrition therapy; OGTT = oral glucose tolerance test; PPG = postprandial glucose; Rx = treatment; SU = sulfonylurea; TZD = thiazolidinedione



\* Available as exenatide  
\*\* Available as pramlintide

<sup>1</sup> Indicated for patients not at goal despite SU and/or metformin or TZD therapy; incretin mimetic is not indicated for insulin-using patients  
<sup>2</sup> For selected patients presenting with an A1C of >10%, certain oral agent combinations may be effective  
<sup>3</sup> Insulin sensitizer may be combined with initial insulin therapy  
<sup>4</sup> Preferred first agent in most patients  
<sup>5</sup> Rapid-acting insulin analog, inhaled insulin, or regular insulin  
<sup>6</sup> Appropriate for most patients  
<sup>7</sup> 2 or more agents may be required  
<sup>8</sup> Analog preparations preferred  
<sup>9</sup> Available as glargine and detemir  
<sup>10</sup> A recent report (NEJM; 6/14/07) suggests a possible link of rosiglitazone to cardiovascular events that requires further evaluation

<sup>†</sup>ACE Glycemic Goals  
 $\leq 6.5\%$  A1C  
 $< 110$  mg/dL FPG  
 $< 110$  mg/dL Preprandial  
 $< 140$  mg/dL 2-hr PPG



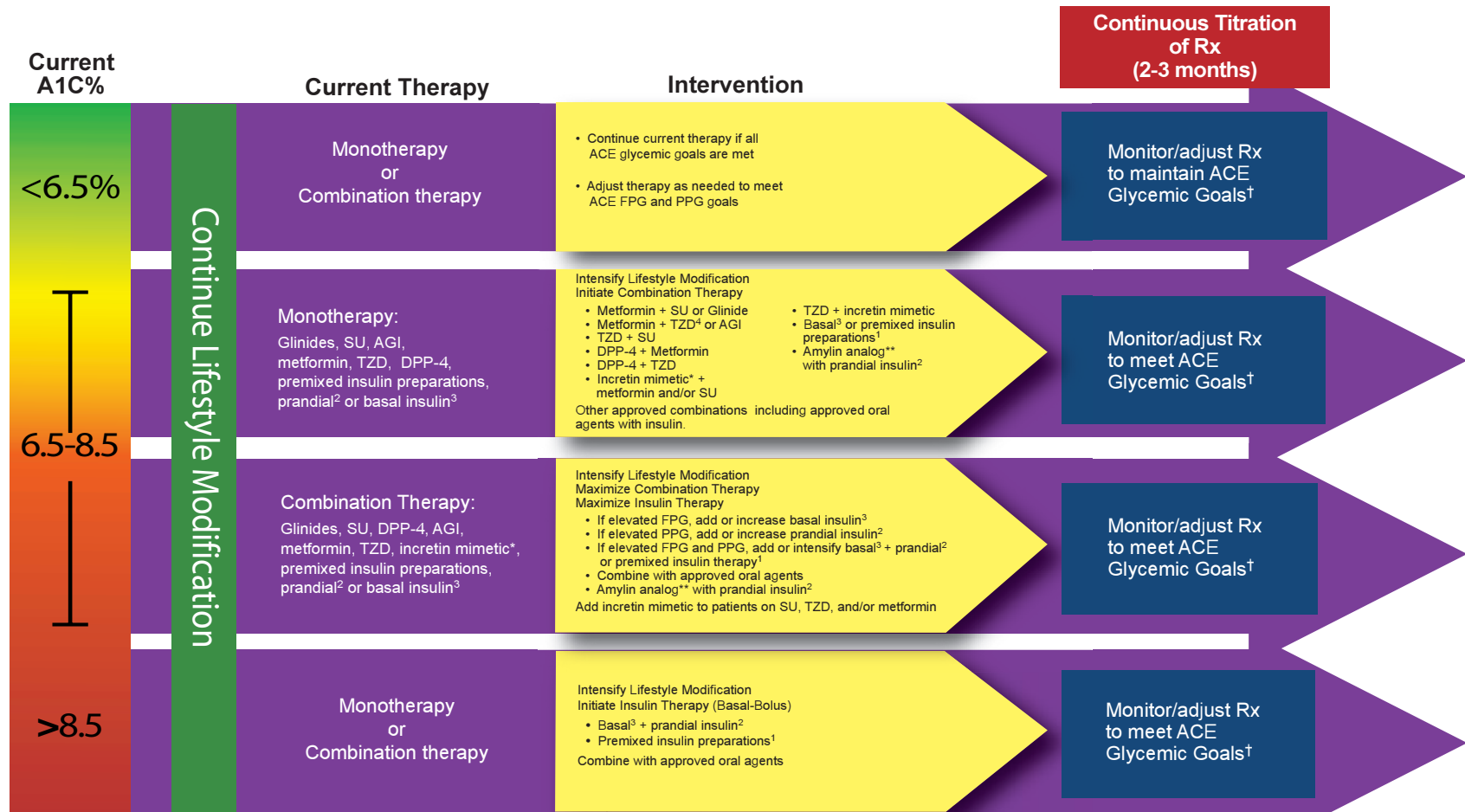
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Fig. 1. Road map to assist clinicians in achieving glycemic goals (established by the American College of Endocrinology and the American Association of Clinical Endocrinologists) in treatment-naïve patients with type 2 diabetes.

# Road Map to Achieve Glycemic Goals: Treated Patients (Type 2)

**Abbreviations in Road Maps:**

AACE = American Association of Clinical Endocrinologists; A1C = hemoglobin A1c; ACE = American College of Endocrinology; AGI =  $\alpha$ -glucosidase inhibitor; DPP-4 = dipeptidyl peptidase-4; FDA = US Food and Drug Administration; FPG = fasting plasma glucose; HDL = high-density lipoprotein; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; MNT = medical nutrition therapy; OGTT = oral glucose tolerance test; PPG = postprandial glucose; Rx = treatment; SU = sulfonylurea; TZD = thiazolidinedione



\* Available as exenatide  
 \*\* Available as pramlintide  
<sup>1</sup> Analog preparations preferred  
<sup>2</sup> Prandial insulin (rapid-acting insulin analog, inhaled insulin, or regular insulin) can be added to any therapeutic intervention at any time to address persistent postprandial hyperglycemia  
<sup>3</sup> Available as glargine and detemir  
<sup>4</sup> A recent report (NEJM; 6/14/07) suggests a possible link of rosiglitazone to cardiovascular events that requires further evaluation

†ACE Glycemic Goals  
 ≤ 6.5% A1C  
 < 110 mg/dL FPG  
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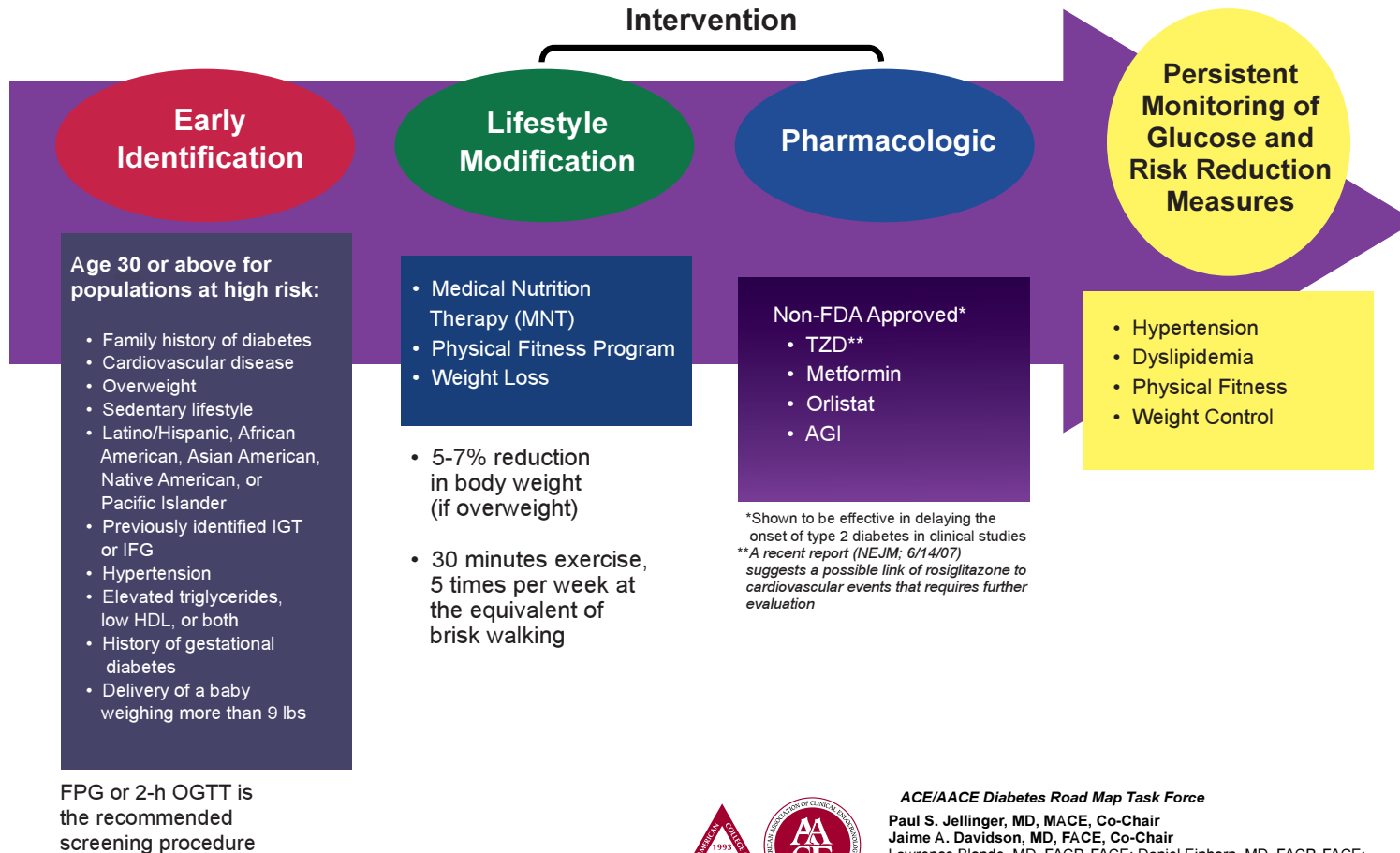
Fig. 2. Road map to assist clinicians in achieving glycemic goals (established by the American College of Endocrinology and the American Association of Clinical Endocrinologists) in treated patients with type 2 diabetes not at hemoglobin A1c goal.

**Fig. 3.** Road map to assist clinicians in prevention of type 2 diabetes, as recommended by the American College of Endocrinology and the American Association of Clinical Endocrinologists.

## Road Map to PREVENT Type 2 Diabetes

### Abbreviations in Road Maps:

**AACE** = American Association of Clinical Endocrinologists; **A1c** = hemoglobin A1c; **ACE** = American College of Endocrinology; **AGI** =  $\alpha$ -glucosidase inhibitor; **DPP-4** = dipeptidyl peptidase-4; **FDA** = US Food and Drug Administration; **FPG** = fasting plasma glucose; **HDL** = high-density lipoprotein; **IFG** = impaired fasting glucose; **IGT** = impaired glucose tolerance; **MNT** = medical nutrition therapy; **OGTT** = oral glucose tolerance test; **PPG** = postprandial glucose; **Rx** = treatment; **SU** = sulfonylurea; **TZD** = thiazolidinedione



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Dr. Yehuda Handelsman has received speaker honoraria from Abbott Laboratories, Amylin Pharmaceuticals, Inc., AstraZeneca, Bristol-Myers Squibb Company, GlaxoSmithKline, Novartis Pharmaceuticals Corporation, and sanofi-aventis and consultant honoraria from Abbott Laboratories, GlaxoSmithKline, and sanofi-aventis. He has also received grant support for research from sanofi-aventis.

Dr. Richard Hellman has received speaker honoraria from Daiichi Sankyo, Inc. and Pfizer Inc. as well as research grants from Abbott Laboratories, Medtronic, Inc., and Pfizer Inc.

Dr. Paul S. Jellinger has received speaker honoraria from GlaxoSmithKline, Merck & Co., Inc., Novartis Pharmaceuticals Corporation, Novo Nordisk Inc., and Takeda Pharmaceuticals America, Inc.

Dr. Harold Lebovitz has received speaker honoraria from GlaxoSmithKline and sanofi-aventis. He has received advisory board honoraria from Amylin Pharmaceuticals, Inc., LifeScan, Inc., and Novartis Pharmaceuticals Corporation. He is a shareholder of Amylin Pharmaceuticals, Inc., Bristol-Myers Squibb Company, and sanofi-aventis stocks.

Dr. Philip Levy has received speaker honoraria from Abbott Laboratories, Amylin Pharmaceuticals, Inc., GlaxoSmithKline, Eli Lilly and Company, Merck & Co., Inc., Novartis Pharmaceuticals Corporation, Novo Nordisk Inc., Pfizer Inc., and sanofi-aventis. He has also received research grants from Amylin Pharmaceuticals, Inc., GlaxoSmithKline, MannKind Corporation, Novo Nordisk Inc., Pfizer Inc., and sanofi-aventis.

Dr. Victor L. Roberts has received speaker honoraria from GlaxoSmithKline, Eli Lilly and Company, Merck & Co., Inc., Novo Nordisk Inc., Pfizer Inc., and sanofi-aventis and has been a speaker for Bristol-Myers Squibb Company and Takeda Pharmaceuticals America, Inc.

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11. Pioglitazone + metformin (Actoplus Met) [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc, 2005. (Not rated)
12. Rosiglitazone (Avandia) [package insert]. Research Triangle Park, NC: GlaxoSmithKline, 2005. (Not rated)