

Online Appendix Figure 1 – Patient Disposition

D/C, discontinued; F-U, follow-up; W/D, withdrawn; Rx, therapy; Non-compl, non-compliance.

	Placebo	5 mg	15 mg	50 mg	100 mg	200 mg				
Ν	50	51	51	46	53	51				
Age, yrs	52 ± 11	55 ± 9	52 ± 10	54 ± 9	54 ± 9	52 ± 10				
Male, n (%)	25 (50)	30 (59)	24 (47)	22 (48)	28 (53)	21 (41)				
Female, n (%)	25 (50)	21 (41)	27 (53)	24 (52)	25 (47)	30 (59)				
Duration T2D, yrs	6.7 ± 6	5.3 ± 5	6.4 ± 5	5.8 ± 5	6.9 ± 6	6.0 ± 5				
Metformin Dose, g/d	1.5 ± 0.5	1.4 ± 0.6	1.5 ± 0.6	1.4 ± 0.5	1.6 ± 0.5	1.6 ± 0.6				
A1c, %	8.3 ± 1	8.2 ± 1	8.3 ± 1	8.3 ± 1	8.2 ± 1	8.2 ± 1				
FPG, mg/dL	179 ± 51	172 ± 41	175 ± 44	178 ± 53	170 ± 64	165 ± 41				
Weight, kg	91 ± 16	91 ± 19	96 ± 22	84 ± 14	89 ± 20	86 ± 17				
BMI, kg/m ²	33 ± 5	33 ± 6	34 ± 5	31 ± 4	32 ± 5	32 ± 5				
Cholesterol, mg/dL	198 ± 52	190 ± 40	177 ± 37	193 ± 54	205 ± 45	194 ± 36				
LDL-C, mg/dL	112 ± 33	107 ± 34	99 ± 345	111 ± 44	121 ± 37	110 ± 27				
HDL-C, mg/dL	49 ± 16	47 ± 13	44 ± 9	46 ± 12	48 ± 10	47 ± 11				
Triglyceride, mg/dL	188 ± 105	189 ± 125	196 ± 153	188 ± 121	187 ± 92	195 ± 127				
sBP, mm Hg	127 ± 12	125 ± 15	127 ± 15	123 ± 11	127 ± 15	125 ± 13				
dBP, mm Hg	78 ± 8	75 ± 8	78 ± 8	76 ± 8	80 ± 8	78 ± 7				
Data are mean + STD unless otherwise noted										

Online Appendix Table 1 – Clinical Characteristics at Baseline

Data are mean \pm STD unless otherwise noted.

Online Appendix Table 2 – Endpoint Electrolyte Assessments

	Ref Range	Placebo	5 mg	15 mg	50 mg	100 mg	200 mg		
Potassium	3.4-5.4 mmol/L	4.4 ± 0.4	4.5 ± 0.4	4.3 ± 0.4	4.3 ± 0.3	4.4 ± 0.4	4.3 ± 0.4		
Sodium	132-147 mmol/L	140 ± 3	142 ± 5	141 ± 3	141 ± 4	142 ± 4	141 ± 3		
Chloride	94-112 mmol/L	102 ± 3	103 ± 4	103 ± 2	102 ± 3	103 ± 3	102 ± 3		
Bicarbonate	17.0-30.6 mmol/L	24.3 ± 2.8	23.9 ± 3.1	24.5 ± 3.2	24.4 ± 3.2	24.4 ± 2.7	24.2 ± 3.4		
Electrolyte data are Week 12 mean ± STD. Central lab normal reference ranges are provided.									

Online Appendix Table 3 – Participating Principal Investigators Andrade, Augustin. Research Physicians Network Alliance; Miami Beach, FL Angles, Luis. Heart of America Research Institute; Shawnee Mission, KS Apantaku, Frank. Illinois Center for Clinical Research; Chicago, IL Armas, Eddie. Well Pharma Medical Research Corporation; South Miami, FL Arshad, Syed. Houston Clinical Research Associates; Houston, TX Bailey, Timothy. North County Endocrine Medical Group; Escondido, CA Banker, Lisa. Carolina Research Trials, PC; New Bern, NC Barker, Timothy. Research Institute of the Carolinas, PLLC; Mooresville, NC Barranco, Elizabeth. Ponce School of Medicine/CAIMED Center; Ponce, Puerto Rico Bartkowiak, Anthony. Blair Medical Associates; Altoona, PA Boeren, John. Belleville Family Medical Associates LTD; Belleville, IL Braun, Edward. Midtown Medical Center; Tampa, FL Brockmyre, Andrew. Holston Medical Group; Bristol, TN Brown, Morris. Laureate Clinical Research Group, LLC; Atlanta, GA Bueso, Gerardo. Endocrine Associates; Houston, TX Cherlin, Richard. Cherlin, Richard MD; Los Gatos, CA Christensen, Tom. Odyssey Research; Calabash, NC Clevinger, Sidney. Renstar Medical Research; Ocala, FL Connery, Lisa. Lynn Health Science Institute; Norman, OK Daryaee, Nader. Southeast Clinical Research, LLC; Chiefland, FL Demetry, Kamal. Midwest Internists Clinical Research, P.C.; St. Louis, MO Fedro, David. First Dynamic Health Care Services, Inc.; Waco, TX Feldman, Gregory; S. Carolina Pharmaceutical Research; Spartanburg, SC Gabra, Nashwa. Burke Internal Medicine; Burke, VA Gabriel, John. North Hills Family Practice; North Richland Hills, TX Gollapudi, Gopalakrishna. Diabetes Center of the Southwest; Midland, TX Henderson, Mark. Acadia Clinical Research, LLC;l Bangor, ME Horowitz, Barry. Metabolic Research Institute, Inc.; West Palm Beach, FL Irizarry, Carmen. Irizarry, Carmen (private practice); Fajardo, Puerto Rico Ison, Rodney. Ison, Rodney, MD; Canal Fulton, OH Jain, Rajeev. Advanced Healthcare, SC-Clinical Research Center; Milwaukee, WI Johary, Albert. Albert Johary, M.D.; Dunwoody, GA Johnson, Glover. Non-Invasive Cardiovascular PA; Santa Ana, TX Kalafer, Marvin. Clinical Trial Center, LLC, Psychiatry; Jenkintown, PA Kerwin, Edward. Clinical Research Institute of Southern Oregon, LLC; Medford, OR Kipnes, Mark. Diabetes & Glandular Disease Research Associates, Inc.; San Antonio, TX Koehler, Lawrence, Wells Institute for Health Awareness; Kettering, OH Kroeze, James. Southwestern Medical Clinic, P.C.; Bridgman, MI Lacour, Audrey. Juno Research, LLC; Houston, TX Landgarten, Steven. Hillcrest Medical Group/Utica Park Clinic; Tulsa, OK Lerman, Sam. Center for Diabetes & Endocrine Care; Hollywood, FL Lesh, Kurt. Lynn Institute of the Rockies; Colorado Spring, CO Levy, Philip. Phoenix Endocrinology Clinic, Ltd.; Phoenix, AZ Lewin, Andrew. National Research Institute; Los Angeles, CA

Littlejohn, Thomas. Piedmont Medical Research Associates; Winston-Salem, NC

Long, William. Neem Research Group of Charlotte; Charlotte, NC

Lorraine, Richard. Harleysville Medical Associates; Harleysville, PA

Lowder, Catherine. St. Louis Center for Clinical Research; St. Louis, MO

Lucas, Mel. Primecare Research Associates; Florissant, MO

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Margolis, Steven. Alternacare, P.C.; Sterling Heights, MI Martin, Earl. Martin Diagnostic Clinic; Houston, TX Matta, Evelyn. Capara Internal Medicine Service Group, Rio Grande, Puerto Rico Mattson, Elizabeth. King's Daughters Clinic; Temple, TX Mays, Brooks, Pinehurst Medical Clinic, Inc.; Pinehurst, NC McCormick, Brian. Hampton Family Practice, PLLC; Hampton, VA Messiha, Magdi. Neuropsychiatric Research Center of Orange County; Santa Ana, CA Moll, David. Grandview Medical Research, Inc.; Sellersville, PA Norwood, Paul. Valley Research; Fresno, CA Only, Ronald. Partners in Family Medicine; Georgetown, TX Patel, Rakesh. DynaMed Clinical Research; Houston, TX Pearson, Darren. St. Louis Center for Clinical Research; St. Louis, MO Pudi, Krishna. Upstate Pharmaceutical Research; Greenville, SC Ramsbottom, John. Odyssey Research; North Myrtle Beach, SC Roberts, Victor. Endocrine Clinical Research; Winter Park, FL Rock, Karin. Greystone Medical Research; Birmingham, AL Rosemore, Michael. Simon-Williamson Clinic, PC; Hueytown, AL Rosenstock, Julio. Dallas Diabetes and Endocrine Center; Dallas, TX Rousseau, Roger. Pharmax Research Clinic, LLC; Miami, FL Saavedra, Rubin. Nevada Alliance Against Diabetes; Las Vegas, NV Sall, Kenneth. Sall Research Medical Center; Artesia, CA Saway, William. Columbia Medical Practice; Columbia, MD Scott, David. Clinical Research Development Associates, LLC; Springfield Gardens, NY Shah, Anil. Medical Helping Hands; Santa Ana, CA Snyder, Brian. Southgate Medical Group; West Seneca, NY Sosa-Padilla, Miguel. Sosa-Padilla, Miguel (private practice); San Juan, Puerto Rico Streja, Dan. Infosphere Clinical Research; Calabasas, CA Tamayo, Raul. Genesis Research International; Longwood, FL Thomas, Flavia. Juno Research, LLC; Houston, TX Toro, Hugo. Juno Research, LLC; Houston, TX Velazquez, Sonia. Clinical Research Puerto Rico, Inc.; San Juan, Puerto Rico Weissman, Peter. Baptist Diabetes Associates Research Center; Miami, FL