

## Supplementary Materials

### List of investigators in ertugliflozin study MK-8835-017

**USA:** John Gabriel, Ted Melliza, Matthew Vela (North Richland Hills, TX); Sam Miller, Rodney Carry (San Antonio, TX); Juan Frias, Stanley Hsia, Sharon Kelly (Los Angeles, CA); David Sandercock, Melissa Kite, Gordon Hill, Clifford Alprin, Walter Walthall (San Antonio, TX); Mario Belledonne (Rockville, MD); Hugo Toro, Amy Megerle, Linda Lin, Miguel Posada (Katy, TX); Audrey Lacour, Linda Lin, Miguel Posada, Alondra Martinez, Rosibel Bustamante, Gilma Martinez (Houston, TX); Baudilio Cusco-Prieto, Virginia Viera (Coral Gables, FL); Rafael Chiong, Mario Jimenez, Sara Llerena (Miami, FL); Cara Dawson (Denver, CO); Eveline Padilla (Hialeah, FL); Jonathan Wise, Howard Miller (Metairie, LA); Michael Seep, William Nabours (Lake Charles, LA); Andrea Lawless, Kathleen Kelley (Addison, IL); Juan Salinas, Lilia Rodríguez Ables, Lilia Rodriguez Ables, Josefina Tur (Miami, FL); Tira Chaicha-Brom, Brandy Wellmon, Lindsay Harrison (Austin, TX); Michael Winnie, Lisa Blair (Corpus Christi, TX); Elias Kolettis, Leonard Dunn, Lynne Merriam, Amy Howard, Melonie Tournai (Clearwater, FL); Mikhail Palatnik, Phillip Ford, Ashley Winters, Diane Battaglia, Kayvan Haddadan, Teri Nguyen, Eric Hanson, Mark Alger (Gold River); Jorge Posada, Alejandro Pla, Carla Vera (Miami Lakes, FL); Eduardo Viera, Roberto Fernandez (Hialeah, FL); Benny Green, Pamela Bariola, Kymberly Amyett (Little Rock, AR); Larry Reed, Keisha Bishop, Brian Springer (Hazelwood, MO); Thomas Ballard, William Byars, Ronald Mayfield, Nancy Durham, Ruth Wood (Greer, SC); Bruce Jackson (Redondo Beach, CA); Jeffrey Klein, Margaret Rhee, Stephanie Wojtowicz, Annette Pangle, Sandra Smith, Stacy Merlitti (Akron, OH); Patricia Buchanan, Douglas Bailey, Dirk deBroekert, Randie Fletcher (Eugene, OR);

Charles Sharpe, Wallace Burroughs (Athens, TN); Debra Weinstein, Reina Mendelson (Boynton Beach, FL); Richard Jackson, Damian Covington (Richmond, VA); Alan Miller, Todd Miller (Dunwoody, GA); Sanjay Vora, Craig Thompson, Marc Comianos (Marion, OH); Ramesh Gupta, Malini Gupta-Ganguli (Memphis, TN); Richard Krause, Andrea Galloway, Rebekah Corey, Brandy Biederman (Chattanooga, TN); Peter Gagianas, Dawnmarie Minyon-Sarver, Anthony Ciampa, John Barrett (McMurray, PA); Deanna Cheung, Leigh Tao, Stephen Zukotynski (Long Beach, CA); David Headley, Jennifer Grear (Port Gibson, MS); Raul Gaona, M. Antonieta Gonzalez (San Antonio, TX); Jack Rosenfeld, Jennifer Craig, Barry Green, William Lee (Lansdale, PA); Carlos Herrera, Samuel Rivera, Robyn Wilson, Ethelina Menchaca (Houston, TX); Douglas Young, Gary Carson, Robin Collins, Narinder Dhaliwal (Sacramento, CA); Rabi Sinha, Grace Silverio (Hopewell Junction, NY); Kaushik Amin (Conyers, GA); Clinton Corder, Cheryl Black (Oklahoma City, OK); Val Hansen, Joseph Jensen (Bountiful, UT); Anthony Captain, Kent Van Arsdell (Calhoun, GA); Stanley Hsia, Juan Frias, Robert Jenders, Sharon Kelly (Huntington Park, CA). **Czech Republic:** Milan Kvapil, Eva Dvorakova, Dagmar Bartaskova, Klaudia Halova Karoliova (Praha); Tomas Brychta, Svetlana Brychtova (Olomouc); Michala Pelikanova, Drahomira Gulakova (Praha); Andrea Gamova, Emilia Malicherova, Eva Roderova, Emilia Malicherova, Petra Jenickova, Karolina Travova (Praha); Petr Maule, Pavla Smejkalova (Humpolec); Juraj Divinec, Zdenek Divis (Pardubice); Richard Zachoval, Danuse Kucerova (Jicin); Dagmar Bartaskova, Jakub Hron (Praha). **Hungary:** Gyöngyi Csécsei, Andrea Filo, Judit Ferenczi, Ildiko Ferencz, Eva Somos, Hortenzia Karolyi, Eva Mihaly, Zsolt Papp (Budapest); Marianna Zsom, Balazs Nyiri, Gabriella Szaboki (Baja); Éva Péterfai, Katalin Bezzegh, Vendel Kemeny, Eniko Kulcsar, Botond Literati Nagy, Jozsef Pauer,

Barbara Buday (Balatonfüred); Peter Danos, Janos Kis, Eleonóra Beke, Andrea Grosz (Budapest); Zsolt Zilahi, Andrea Nagy (Nyregyhza). **Israel:** Julio Wainstein Maya Ish Shalom (Tel Aviv); Deeb Daoud, Irit Hochberg, Sagit Zolotov, Moshe Zloczower, Elena Segal (Haifa). **United Kingdom:** Mark Blagden, Jahanzeb Ali (Chesterfield); Charles Bundy, Karamjeet Bimbh, Stephen Locke (Trowbridge); Richard Gaunt, Gavin Durrant, Alistair McKibbin (Chippenham); Venkata Kondagunta, Judith Mackay, Devinda Weeraratne, Daniela Hristova (Reading); Paul Ivan, Essam Eldin Ahmed Abdulhakim, Susannah Eyre (Liverpool); Fiona Douglas (Hexham); Hawys Thomas, Maria Rita Charters (Cardiff); Surabhi Gunput, Giuseppe Fiore Paul Ivan, Tomas Ko (Chorley); Helen Timmis, Mohamed Okily, Mohamed Okily, Madhu Venkate Gowda (Manchester); Amit Mathew, Babatunde Oyesile, Anton Poterajlo (Edgbaston); Veronika Horvathova, Imrozia Arif, Devinda Weeraratne, Imrozia Arif, Anthony Avornyo (Glasgow). **Ukraine:** Halyna Myshanych, Tetiana Zalievska, Oleh Myshanych, Nataliya Bazhenova, Svitlana Samoilo, Yaroslav Kleban (Kyiv); Inna Sorokina, Oleksandra Donets, Svitlana Postol, Ievgeniia Tokareva, Oleksandra Bilotkach (Kyiv). **Bulgaria:** Emiliya Apostolova, Momchil Hubchev (Smolyan); Georgi Levterov, Katya Doykova, Milen Yosifov (Plovdiv); Nadezhda Ivanova Mendizova, Vladimir Vasilev (Sofia). **Serbia:** Nebojsa Lalic, Aleksandra Jotic, Ljiljana Lukic, Tanja Milicic, Marija Macesic, Jelena Seferovic, Milica Prostran, Jelena Stanarcic Gajovic (Belgrade); Dragan Micic, Aleksandra Kendereski, Goran Cvijovic, Snezana Polovina, Milica Prostran (Belgrade); Katarina Lalic, Natasa Rajkovic, Ljiljana Popovic, Sandra Singh, Ljubica Stosic, Milica Prostran (Belgrade); Dragan Dimic; Milena Velojic-Golubovic (Nis); Milica Pesic, Danijela Radojkovic, Sonja Kostic (Nis); Slobodan Antic, Danijela Stojic (Nis); Edita Stokic, Bojan Vukovic, Jovanka Novakovic-Paro, Branka Kovacev-

Zavisić, Slobodan Mijačević (Novi Sad); Aleksandar Djukić, Jelena Petrović, Violeta Mladenović, Dragana Bubanja (Kragujevac). **Croatia:** Srećko Tušek, Nedjeljko Ciglenceki (Toplice); Lea Smirčić Duvnjak, Dragica Soldo, Anica Badanjak, Tomislav Božek (Zagreb); Zeljka Crncević-Orlić, Nina Poropat (Rijeka); Dario Rahečić, Petra Melis (Zagreb); Silvija Čanečki-Varžić, Vedrana Baraban (Osijek). **Estonia:** Kaja Martsin, Olga Basulina (Tallinn); Kaia Kiiroja, Margit Venesaar (Tallinn); Riin Lanno, Elina Šel'pakova, Mare Vilberg (Tallinn); Kaja Arbeiter, Mirjam Turkson (Tallinn); Ingrid Alt, Kulli Paju (Paide).

**Supplementary Table S1** Glycated hemoglobin (HbA1c) distribution at baseline and subgroup efficacy analysis (change in HbA1c from baseline at week 26 per baseline HbA1c)

	<b>Placebo</b>	<b>E5/S100</b>	<b>E15/S100</b>
Baseline HbA1c ≤ median HbA1c (9.0% [75 mmol/mol])	<b>n = 46</b>	<b>n = 53</b>	<b>n = 49</b>
HbA1c distribution at baseline, % (mmol/mol)	8.3 (67.0)	8.3 (67.2)	8.3 (67.7)
LS mean change from baseline at week 26, % (95% CI)	-0.0 (-0.4, 0.3)	-1.4 (-1.7, -1.1)	-1.3 (-1.6, -1.0)
<i>LS mean change from baseline at week 26, mmol/mol (95% CI)</i>	-0.3 (-3.9, 3.3)	-15.5 (-18.6, -12.4)	-14.2 (-17.4, -11.0)
Difference in LS mean change vs. placebo, % (95% CI)	-	-1.4 (-1.8, -1.0)	-1.3 (-1.7, -0.8)
<i>Difference in LS mean change vs. placebo, mmol/mol (95% CI)</i>	-	-15.2 (-20.0, -10.5)	-13.9 (-18.7, -9.1)
Baseline HbA1c > median HbA1c (9.0% [75 mmol/mol])	<b>n = 39</b>	<b>n = 44</b>	<b>n = 43</b>
HbA1c distribution at baseline, % (mmol/mol)	9.8 (83.1)	9.6 (81.8)	9.8 (83.1)
LS mean change from baseline at week 26, % (95% CI)	-1.0 (-1.4, -0.6)	-1.8 (-2.1, -1.5)	-2.2 (-2.5, -1.9)
<i>LS mean change from baseline at week 26, mmol/mol (95% CI)</i>	-10.9 (-15.0, -6.7)	-19.7 (-23.2, -16.2)	-24.3 (-27.8, -20.8)
Difference in LS mean change vs. placebo, % (95% CI)	-	-0.8 (-1.3, -0.3)	-1.2 (-1.7, -0.7)
<i>Difference in LS mean change vs. placebo, mmol/mol (95% CI)</i>	-	-8.9 (-14.3, -3.4)	-13.4 (-18.8, -8.0)

*CI* confidence interval *E* ertugliflozin *LS* least squares *S* sitagliptin

**Supplementary Table 2** Additional secondary efficacy endpoints at week 26<sup>a</sup>

	Placebo	E5/S100	E15/S100
Glycemic rescue medication	<i>n</i> = 97	<i>n</i> = 98	<i>n</i> = 96
Number of patients, <i>n</i> (%)	31 (32.0)	6 (6.1) <sup>b</sup>	0 (0.0) <sup>b</sup>
HOMA-β, %	<i>n</i> = 90	<i>n</i> = 97	<i>n</i> = 96
LS mean change from baseline (95% CI)	4.1 (−1.7, 10.0)	20.6 (15.7, 25.5)	24.3 (19.4, 29.1)
Pairwise comparison vs. placebo, difference in LS means (95% CI)	–	16.5 (9.1, 23.9) <sup>b</sup>	20.1 (12.7, 27.6) <sup>b</sup>
Insulinogenic index, ng/mL per mg/dL	<i>n</i> = 90	<i>n</i> = 97	<i>n</i> = 95
LS mean change from baseline (95% CI)	0.0 (−0.02, 0.03)	0.02 (0.00, 0.04)	0.03 (0.01, 0.05)
Pairwise comparison vs. placebo, difference in LS means (95% CI)	–	0.02 (−0.01, 0.05)	0.03 (−0.00, 0.06)
Patients with HbA1c <6.5% (<48 mmol/mol)	<i>n</i> = 96	<i>n</i> = 98	<i>n</i> = 96
Number of patients, <i>n</i> (%)	4 (4.2)	25 (25.5)	17 (17.7)
Adjusted odds ratio relative to placebo (95% CI)	–	12.3 (3.2, 46.9) <sup>b</sup>	8.1 (2.1, 31.1) <sup>c</sup>

<sup>a</sup>These secondary efficacy analyses were not included in the ordered testing procedure and nominal *p* values are provided for descriptive purposes only; <sup>b</sup>*p* < 0.001 vs.

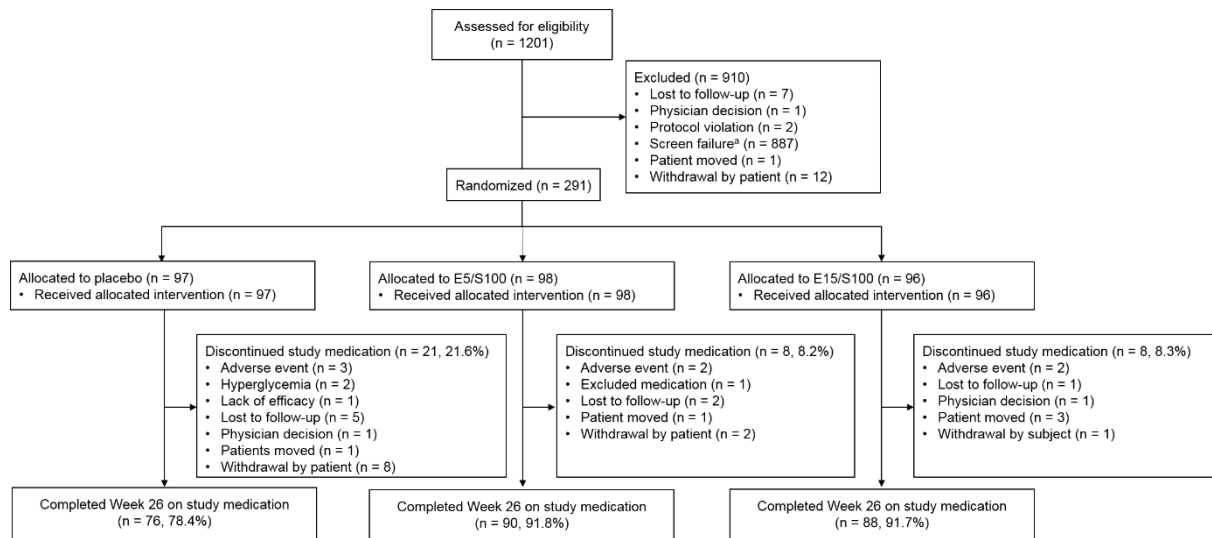
placebo; <sup>c</sup>*p* = 0.002 vs. placebo. *CI* confidence interval *E* ertugliflozin *HbA1c* glycated hemoglobin *HOMA-β* homeostasis model assessment of β-cell function *LS* least squares *S* sitagliptin.

**Supplementary Table S3** Percent change in low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) from baseline at week 26

	<b>Placebo</b>	<b>E5/S100</b>	<b>E15/S100</b>
<b>LDL-C</b>	<i>n</i> = 68	<i>n</i> = 86	<i>n</i> = 86
LS mean percent change from baseline (95% CI)	2.9 (−3.5, 9.2)	10.6 (4.9, 16.3)	10.1 (4.4, 15.8)
Pairwise comparison vs. placebo, difference in LS means (95% CI)	–	7.7 (−0.6, 16.1)	7.2 (−1.1, 15.6)
<b>HDL-C</b>	<i>n</i> = 68	<i>n</i> = 86	<i>n</i> = 88
LS mean percent change from baseline (95% CI)	3.6 (−0.3, 7.5)	9.3 (5.8, 12.7)	8.2 (4.8, 11.6)
Pairwise comparison vs. placebo, difference in LS means (95% CI)	–	5.7 (0.5, 10.9)	4.6 (−0.5, 9.8)

*CI* confidence interval *E* ertugliflozin *LS* least squares *S* sitagliptin

## Supplementary Fig. S1 Patient disposition



### E ertugliflozin S sitagliptin

<sup>a</sup>The most common reasons for screen failure were not meeting the inclusion criteria for HbA1c at Visit 1 relative to a patient's category of background diabetes therapy, and having exclusionary laboratory values.