**Supplementary Materials**

**Supplemental Methods**

The empagliflozin/linagliptin/metformin extended release (metformin XR) fixed dose combination tablets were manufactured by Patheon Pharmaceuticals, Inc., Cincinnati, USA. Jardiance® (10 mg empagliflozin immediate release tablet) and Tradjenta® (5 mg linagliptin immediate release tablet) were US commercial products and marketed by BI Pharmaceuticals, Inc., Ridgefield, USA, and Eli Lilly and Company, Indianapolis, USA. Glumetza® (500 mg metformin hydrochloride extended release tablet) was a US commercial product and manufactured for Salix Pharmaceuticals, a division of Valeant Pharmaceuticals North America LLC, Bridgewater, USA. Management of clinical study supplies (including ordering, labelling, and distribution) was performed by the Clinical Trial Supplies Unit of Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach, Germany.

The medication was administered as a single oral dose together with 240 mL of water to a subject in the standing position under supervision of the investigating physician or an authorized designee. The so-called four-eye principle (two-person rule) was applied for administration of trial medication. Participants were kept under close medical surveillance until 24 h following drug administration. During the first 5 h after drug administration, study participants were not permitted to lie down (that is, no declination of the upper body of more than 45 degrees from upright posture).

In each treatment period, a high-fat, high-calorie meal was served 30 minutes before drug administration. The meal had to be completely consumed prior to drug administration. The composition of the standard high-fat, high-calorie meal was in compliance with the FDA requirements.

During sample collection, the dates and times of drug administrations as well as of pharmacokinetic sampling were recorded. Exact time points of plasma sampling were derived from the study management system ClinBase™ and documented by the medical personnel or sent as electronic files to the trial data manager. The actual sampling times were used for determination of pharmacokinetic parameters.

For quantification of empagliflozin, linagliptin, and metformin plasma concentrations, 7.5 mL of blood was taken at each sampling time point from an antecubital or forearm vein into a K3-EDTA (tripotassium ethylenediaminetetraacetic acid)-anticoagulant blood drawing tube. Blood was withdrawn by means of either an indwelling venous catheter or by venipuncture with a metal needle. The EDTA-anticoagulated blood samples were centrifuged for about 10 min at about 2000 to 4000 x g and at 4 to 8°C. Six plasma aliquots (2 aliquots each for empagliflozin, linagliptin, and metformin analysis) were obtained and stored in polypropylene tubes. The first aliquots were to contain at least 0.5 mL plasma. The process from blood collection until transfer of plasma aliquots into the freezer was to be completed within 90 minutes, with interim storage of blood samples in ice water or on ice. For each aliquot, the time when the sample was placed in the freezer was to be documented. Until transfer on dry ice to the analytical laboratories, the aliquots were stored upright at about ‒20°C or below at the trial site. The second aliquots were shipped to the analytical laboratories after the analyst had acknowledged safe arrival of the first aliquots. At the analytical laboratories, the plasma samples were stored at about ‒20°C or below until analysis.

Empagliflozin concentrations in plasma were determined by a validated liquid chromatography tandem mass spectrometry (LC-MS/MS) assay at clinical research organization, BASi (Bioanalytical Systems Inc.), West-Lafayette, USA. Linagliptin concentrations in plasma were determined by a validated LC-MS/MS assay at Covance Laboratories Ltd., Harrogate, UK. Metformin concentrations in plasma were determined by a validated LC-MS/MS assay at SGS Cephac Europe, Saint Benoît Cedex, France. During sample analysis, analysts were blinded to subject allocation and had no access to the random code.