Supplemental Table Study Inclusion and Exclusion Criteria

	First-in-Man	PK/PD study
Inclusion Criteria	• Written informed consent must be obtained before any assessment is performed • Male and female subjects ≥18 years of age, with body weight <120 kg and body mass index (BMI) <30 kg/m^2 • Female subjects must be at least 2 years post-menopausal • Participant must have been on oral furosemide (40 mg oid or bid) or therapeutic equivalent (bumetanide 1 mg oid or bid) for a period 90 days before the first dose of study medication • History of chronic heart failure according to 2012 ESC guidelines with presence of moderate symptoms of chronic fluid overload. Chronic fluid overload is defined as presence of stable signs and symptoms of heart failure and congestion, such as dyspnea at mild exertion or minimal exertion, pulmonary congestion and/or peripheral edema at the time of presentation in combination with elevated levels on natriuretic peptides (NT-proBNP > 300 pg/mL) • In the opinion of the investigator, able to participate in the study	• An Institutional Review Board (IRB) approved informed consent is signed and dated prior to any study-related activities. • Male and female subjects ≥18 years of age, with body volume and weight <130 kg and body mass index (BMI) <34 kg/m^2 • Females will be non-pregnant, non-lactating, and either post-menopausal or surgically sterile (e.g., tubal ligation, hysterectomy), or use two (2) forms of contraception or abstinence. • • History of at least 3 months treated heart failure (NYHA class II/III) with presence of symptoms of chronic fluid overload requiring ongoing treatment with oral furosemide at a dose of ≥40 mg per day for at least 30 days prior to baseline. • Agrees to abstain from using alcohol, caffeine-containing products, and tobacco-/nicotine-containing products through CRU discharge (period 2). • Able to participate in the study in the opinion of the investigator • Has the ability to understand the requirements of the study and is willing to comply with all study procedures.

Exclusion Criteria	• Acute Decompensated Heart Failure (ADHF) or recent history of ADHF or significant worsening in their HF symptoms (within prior 2 weeks) • Contraindication to furosemide • Systolic BP (SBP) < 90 mm Hg • Temperature > 38°C (oral or equivalent) or sepsis or active infection requiring i.v. anti-microbial treatment • Serum sodium < 130 mEq/L and Serum potassium < 3.0 mEq/L • Current or planned (throughout the completion of study drug infusion) treatment with any i.v. therapies, including inotropic agents, vasopressors, levosimendan, nesiritide or analogues; or mechanical support (intra-aortic balloon pump, endotracheal intubation, mechanical ventilation, or any ventricular assist device) • History of gastric or intestinal surgery that may affect absorption of oral medication • Presence or need for urinary catheterization • Current or planned ultrafiltration, hemofiltration, or dialysis • Impaired renal function defined as an estimated glomerular filtration rate (eGFR) on admission < 30 mL/min/1.73 m^2, calculated using the simplified Modification of Diet in Renal Disease (sMDRD) equation • Administration of intravenous radiographic contrast agent within 72 hours prior to screening or acute contrast-induced nephropathy at the time of screening • Major surgery within 30 days prior to screening • Administration of an investigational drug or implantation of	• Acute Decompensated Heart Failure (ADHF) or recent hospitalization for heart failure in the last 4 weeks. • Worsening of signs or symptoms of heart failure in the two weeks prior to the Screening, or those expected to require intravenous loop diuretics or in-patient treatment for heart failure during the study. • History of chronic skin conditions requiring medical therapy • Systolic BP (SBP) < 90 mm Hg • Temperature > 38°C (oral or equivalent) or sepsis or active infection requiring IV anti-microbial treatment • Serum sodium < 130 mEq/L and Serum potassium < 3.0 mEq/L • Significant other cardiac abnormalities that may interfere with study participation or study assessments • Current or planned treatment during the study with any IV therapies, including inotropic agents, vasopressors, levosimendan, nesiritide or analogues; or mechanical support (intra-aortic balloon pump, endotracheal intubation, mechanical ventilation, or any ventricular assist device) • Diagnosed with Type I diabetes mellitus or Type II diabetes requiring insulin therapy • Presence or need for urinary catheterization, urinary tract

	investigational device, or participation in another trial, within 30 days before screening • Inability to follow instructions or comply with procedures • Any surgical or medical condition which in the opinion of the investigator may interfere with participation in the study or which may affect the outcome of the study	abnormality, or disorder interfering with urination • Impaired renal function, defined as an estimated glomerular filtration rate (eGFR) on admission < 45 mL/min/1.73m^2, calculated using the simplified Modification of Diet in Renal Disease (sMDRD) equation • Indication of moderate-to-severe hepatic dysfunctions as determined by the investigator. • Administration of intravenous radiographic contrast agent within 72 hours prior to Screening or acute contrast-induced nephropathy at the time of Screening • Major surgery within 30 days prior to Screening • Administration of an investigational drug or implantation of investigational device, or participation in another trial, within 30 days prior to Screening • Any surgical or medical condition which in the opinion of the investigator may interfere with participation in the study or which may affect the outcome of the study • Positive test for hepatitis B, hepatitis C, or HIV at Screening. • Positive urine drug screen at Screening or Baseline • Concomitant use of any drugs known to interact with furosemide • History of alcohol abuse within 6 months prior to

		screening, as determined by the Investigator • Positive alcohol breath test on admission to the CRU. • History of severe allergic or hypersensitivity reactions to furosemide • Donation of greater than 100 mL of either whole blood or plasma within 30 days prior to study drug administration.