FINAL – Approved for Release

# scPharmaceuticals Announces Positive Results from Pivotal Trial of its Novel Subcutaneous Furosemide Formulation in Patients with Heart Failure

***– Complete (100%) bioavailability after subcutaneous administration when compared with intravenous administration –***

***– Diuresis at 8 and 24 hours was equivalent to diuresis following standard intravenous administration***

***– U.S. and EU regulatory filings anticipated in 2016 –***

LEXINGTON, MA. – scPharmaceuticals, Inc. today announced positive results from its pharmacokinetic and pharmacodynamics phase 3 pivotal registration trial. The trial in patients with heart failure compared subcutaneous administration of a novel furosemide formulation with intravenous administration of furosemide USP (the commercial reference product). Furosemide is a diuretic; it induces urine output to reduce fluid overload (edema), a hallmark of heart failure. The trial results indicated that the subcutaneous administration of the novel furosemide formulation was as effective as the traditional intravenous administration in getting furosemide into the blood stream, and in achieving diuresis. The subcutaneous administration used a proprietary biphasic delivery profile. The reference treatment was commercial furosemide injection, USP administered intravenously in accordance with its prescribing information.

The cross-over study was designed to provide an accurate estimate of bioavailability after subcutaneous administration. Bioavailability refers to the proportion of the administered dose that can be found in the blood stream. Bioavailability following intravenous administration is considered 100%. FDA reviewed the protocol prior to the start of the study.

scPharmaceuticals reports the following results:

| | *scPharmaceuticals' furosemide formulation* | *Furosemide injection, USP* |
|---|---|---|
| *Administration* | Subcutaneous Administration – 80mg by biphasic delivery | Intravenous Administration – 2x 40mg IV at t0 and t2h |
| *Bioavailability (t:0-24h)* | 100%* | 100% |
| *Diuresis 0-8 hours* | 2,654 ml | 2,610 mL |
| *Diuresis 0-24 hours* | 3,630 mL | 3, 538 mL |

* calculated bioavailability was 102%

This study is part of scPharmaceuticals' development program for the sc2Wear Furosemide Patch Pump, a proprietary patch pump for subcutaneous administration of the novel furosemide formulation. Subcutaneous administration in this trial used a proprietary biphasic delivery profile. A total of 10mL of the novel furosemide formulation (8mg/mL) was administered over five hours with 30mg in the first

hour and 12.5mg/hour for the remaining four hours. The drug was delivered via a very small needle (27G) that penetrates the skin of the abdominal wall. No drug-induced skin-irritation or discomfort was observed. The study details and complete results are expected to be published in a medical journal in 2016.

Furosemide is the most widely used injectable cardiovascular drug with approximately 30M units administered in the US alone. With rare exception, furosemide injections are given intravenously by inserting a cannula in a vein of the hand or forearm. Placing an IV cannula, unlike phlebotomy, is an invasive procedure that may only be performed by certified healthcare professionals, such as nurses, EMT and physicians. Subcutaneous administration is easier, less painful, and can often be performed by patients, caregivers and non-certified healthcare professionals such as medical assistants.

“These results confirm that we can achieve “IV-like” diuresis with subcutaneous administration of the novel furosemide formulation”, said Pieter Muntendam, MD, President and CEO of scPharmaceuticals. “One in three Medicare dollars is spent on patients with heart failure with close to 60% of this for inpatient care. This novel option would facilitate more prompt diuresis management to avoid hospital admissions or finish treatments at home to reduce length of stay”.

“Addressing unsustainable health care costs requires innovative, cost-saving technologies that better manage and treat common, serious, and expensive medical conditions", said Leonard Schaeffer, a member of the scPharmaceuticals Board of Directors, founding Chairman and CEO of WellPoint (now Anthem), and previous Administrator of the Health Care Financing Administration (HCFA – now CMS). “Payers are targeting high-cost conditions, such as heart failure, where there is opportunity to improve care. scPharmaceuticals’ subcutaneous furosemide product is being developed in response to the incentives to treat heart failure patients more promptly and efficiently in lower cost care settings.”

“Over the past 50 years, improvements in heart failure management have been incremental, not transformative” said Bertram Pitt, MD, Professor of Medicine Emeritus at the University of Michigan and co-founder of scPharmaceuticals. “The demonstration that the subcutaneous administration of furosemide can mimic the effects of IV administration enables a new care model for effective prevention and treatment of fluid overload outside high-cost care centers. When adopted, this could markedly reduce hospital admissions and readmissions for heart failure thereby increasing patient satisfaction and reducing health care costs.”

scPharmaceuticals is in an advanced stage of developing its drug-device combination product that is subject to FDA’s 505(b)(2) NDA review and approval procedure prior to introduction. scPharmaceuticals expects to submit the NDA in mid-2016. International regulatory filings are anticipated for the second half of 2016.

**About Furosemide**

Furosemide is the most widely used diuretic in heart failure. It is the active ingredient of Lasix®. Furosemide has been in widespread clinical use for almost 50 years. The majority of heart failure patients use furosemide in tablet form on a daily basis to prevent fluid build-up. Despite oral treatment with furosemide, fluid build-up may happen from time to time as a result of dietary transgression (excess salt intake) or poor medication compliance, or for unknown reasons. Once fluid overload occurs, the excess fluid may interfere with absorption of oral medication, further aggravating the fluid overload.

Fluid overload increases symptoms of heart failure and may cause emergency situations. Removal of excess fluid by means of IV furosemide is the cornerstone of treating fluid overload -or edema- in heart failure. The typical patient loses more than 2 gallons (8.4± 5.2L) during a hospital stay, resulting in a weight loss of more than 15 pounds (6.9 ±5.2kg) during the average hospital stay.[1]

**About the scPharmaceuticals Furosemide Formulation and Delivery**

Furosemide is insoluble in water but readily dissolves in alkaline fluids. Commercial furosemide products for injection (furosemide injection, solution, USP) are alkaline (pH 8.3-9.0). When injected under the skin, alkaline fluids may cause skin irritation and discomfort. scPharmaceuticals' research led to the discovery and development of a novel furosemide formulation with the same acidity as the human body (pH 7.4). The proprietary biphasic delivery profile was designed by experts in the field of heart failure to achieve therapeutic levels (blood levels at which furosemide induces diuresis) in approximately 30 minutes and maintain these levels for approximately 5 hours.

**About Heart Failure**

Heart failure is a chronic, progressive, heterogeneous condition in which the heart muscle is unable to pump enough blood through to meet the body's needs for blood and oxygen. Basically, the heart can't keep up with its workload. One of the hallmarks of heart failure is retention of water and salt, resulting in fluid overload. Fluid overload causes accumulation of fluid under the skin (edema) and worsening of symptoms, most notably shortness of breath.

Heart failure is common. An estimated 5.7 million Americans have heart failure. Projections show that the prevalence of heart failure will increase 46% to over 8 million people by the year 2030.[2]

Patients with heart failure are responsible for 34% of Medicare spending as a result of very high rates of hospital admission: patients with heart failure are responsible for 42% of all Medicare hospital admissions and 55% of readmissions.[3]

**Important Information**

The scPharmaceuticals furosemide formulation and sc2Wear Patch Pump are subject to FDA and other regulatory review and approval prior to commercial introduction and clinical use.

**About scPharmaceuticals**

scPharmaceuticals, Inc. based in Lexington, MA, is a privately held biopharmaceutical company developing a portfolio of transformative pharmaceutical products for subcutaneous delivery. Our innovative products are based on widely used generic drugs that currently require intravenous or intramuscular injections. They will be administered subcutaneously via the sc2Wear Pump. This avoids material risks and costs associated with the current delivery options. Our lead products are the first subcutaneous formulation of furosemide (the most widely used parenteral diuretic in treating heart

failure), and ceftriaxone (the parenteral antibiotic most widely used outside the hospital setting). Our novel furosemide formulation enables convenient anytime anywhere use, for example in an outpatient setting instead of the emergency room or other in-patient settings. For ceftriaxone and other antibiotics, subcutaneous administration eliminates the need for PICCs (peripherally inserted central catheters), which are associated with serious complications, frequent adverse events and high medical costs. For further information on how we are transforming the administration of parenteral drugs, go to www.scpharmaceuticals.com.

**References**

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2. Mozaffarian D, et al.; on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Heart disease and stroke statistics—2015 update: a report from the American Heart Association*. Circulation. 2015 Jan 27;131(4):e29-322.
3. Milliman. *The high cost of heart failure for health systems: Opportunities for better management*. By Bruce S. Pyenson, Kathryn V. Fitch, Tyler Engel | 22 July 2015. http://us.milliman.com/uploadedFiles/insight/2015/high-cost-heart-failure.pdf.

**Contact Information:**

Katherine Taudvin
Director, Corporate Development
Email: ktaudvin@scpharma.com
Telephone: (781) 301-6706