SERODUS

Diabetic Kidney Disease

Significant, Focused Market

SER150 - Lead compound in Phase 2/3

May 2023

SER150
Executive Summary

SER150 Halts progression of Diabetic Kidney Disease	
Mode of Action	Dual mode of action: Thromboxane A2 (TXA2) receptor antagonist and Thromboxane synthase inhibitor
API	New Molecular Entity, small molecule
Administration	Oral
Formulation	Capsule
IP	Composition-of-matter patent, priority date 2008. Medical Use patent, expires 2040
CMC	Scalable manufacturing process established for both Drug Substance and Product
Status	Phase 2: Finalized in patients with Diabetic Kidney Disease Clinical Proof of Concept obtained Decrease in albuminuria is statistically significant No safety or tolerability concerns Phase 2/3: Ongoing clinical study SER150 6 months dosing

SER150

A Thromboxane Receptor Antagonist
&
A Thromboxane Synthase Inhibitor

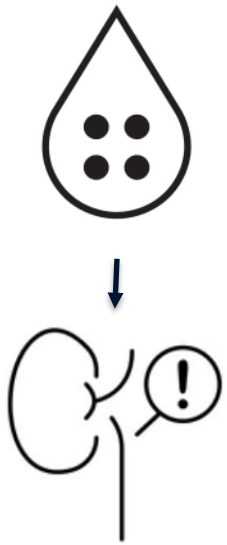
SER150
Repositioning

SER150 is repositioned from being

an anticoagulant candidate

to

being a low-grade anti-inflammatory compound



First indication is Diabetic Kidney Disease

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Diabetic Kidney Disease
Characteristics

- An important complication of Type 2 Diabetes
- Elevated blood sugar triggers inflammatory processes that damage kidneys
- Urinary albumin is a strong biomarker of kidney disease
- Leading cause of end-stage renal disease
- Loss of kidney function ↑ morbidity and ↑ cardiovascular mortality

Reference: ADA Consensus Conference. Diabetes Care 2014

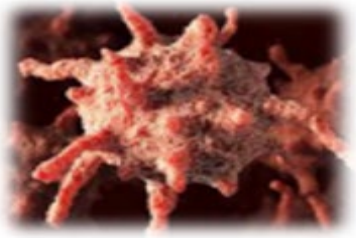
Thromboxane and Thrombocytes

Keys of low-grade Inflammation in Diabetic Patients

Activated thrombocytes and macrophages accumulate in diabetic kidneys

	Non-diabetics	Diabetics
Thromboxane (TXA_2)	~	↑
Cytokines: IL-1, IL-6	~	↑
TXA_2 synthase in thrombocytes	~	↑↑
TXA_2 receptor self-activation	~	↑
Tumor necrosis factor (TNFα)	~	↑↑
TNF Receptor1 (pro-inflammatory)	~	↑↑
TNF Receptor 2 (anti-inflammatory)	~	↓↓
Aspirin sensitivity	~	↓

Diabetic activated thrombocyte



~ : normal level

↑ : increased level

↓ : decreased level

Also, macrophages are activated in diabetes

Thrombocytes are activated and increases number of TNFα receptors

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Ref: Davi 1997, Sterne 1998, Schneider 2009, Israels 2014, Santilli 2010, Angiololo 2011, Shyamkrishnan 2021

Distribution of Thromboxane Receptor and Thromboxane Synthase

Thromboxane A 2 (TxA2) is a potent derivative of arachidonic acid
Arachidonic acid is an integrated constituent of biological cell membrane

Thromboxane receptors are localized in the kidney:
Glomerular capillaries
Glomerular epithelial cells and podocytes
Luminal surface of thick ascending and distal convoluted tubules

Thromboxane receptors are localization outside the kidney:
Platelets, Lung, Vascular smooth muscle, Brain, Spleen, Thymus, Macrophages, Uterus and placenta

Thromboxane synthase is localized:
Platelets, Monocyte/Macrophage, renal interstitial mesangial cells, podocytes.

Ref: Nürsing 1994Abe 1995, Bresnahan 1996, Haluska 2000

Serodus clinical studies in patients

with

Diabetic Kidney Disease

SER150
CL-007 Study Design

Study Design

Randomised, double blind, placebo-controlled, dose-escalation study

Primary Endpoint

Safety & Tolerability

Secondary Parameters

Change in urine albumin excretion

Dosing

One month, twice daily

Study Organization

72 patients participated in the study at 10 centers in Germany

Patient Characteristics

Type 2 Diabetic patients with stable blood glucose and ACR > 30 mg albumin/g creatinine

Cohort 1	25 SER150 12 Placebo	15 mg BID
Cohort 2	24 SER150 11 Placebo	30 mg BID

Screening → **Baseline** → **4 weeks**

- Urine albumin
- Safety parameters

- Urine albumin
- Safety parameters

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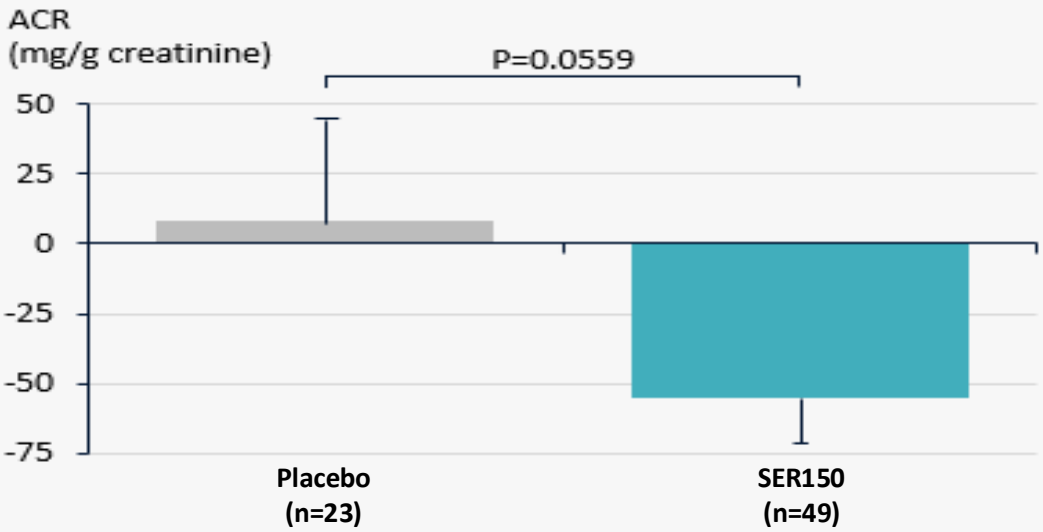
Ref: SER150 CL-007

ACR: Urine albumin corrected for creatinine

SER150 – Clinical Proof of Concept

Change in ACR* ratio from baseline to 4 weeks



SER150 dose	
SER150 15 mg BID** decreased ACR 29.9% from baseline	*P=0.02*
SER150 30 mg BID decreased ACR 20.2% from baseline	*P=0.04*
No significant difference between the doses	

<u>Inclusion criteria:</u>

ACR > 30 mg/g

Normal:

- blood glucose
- kidney function
- treated with ACE or ARB

Ref: SER150 CL-007

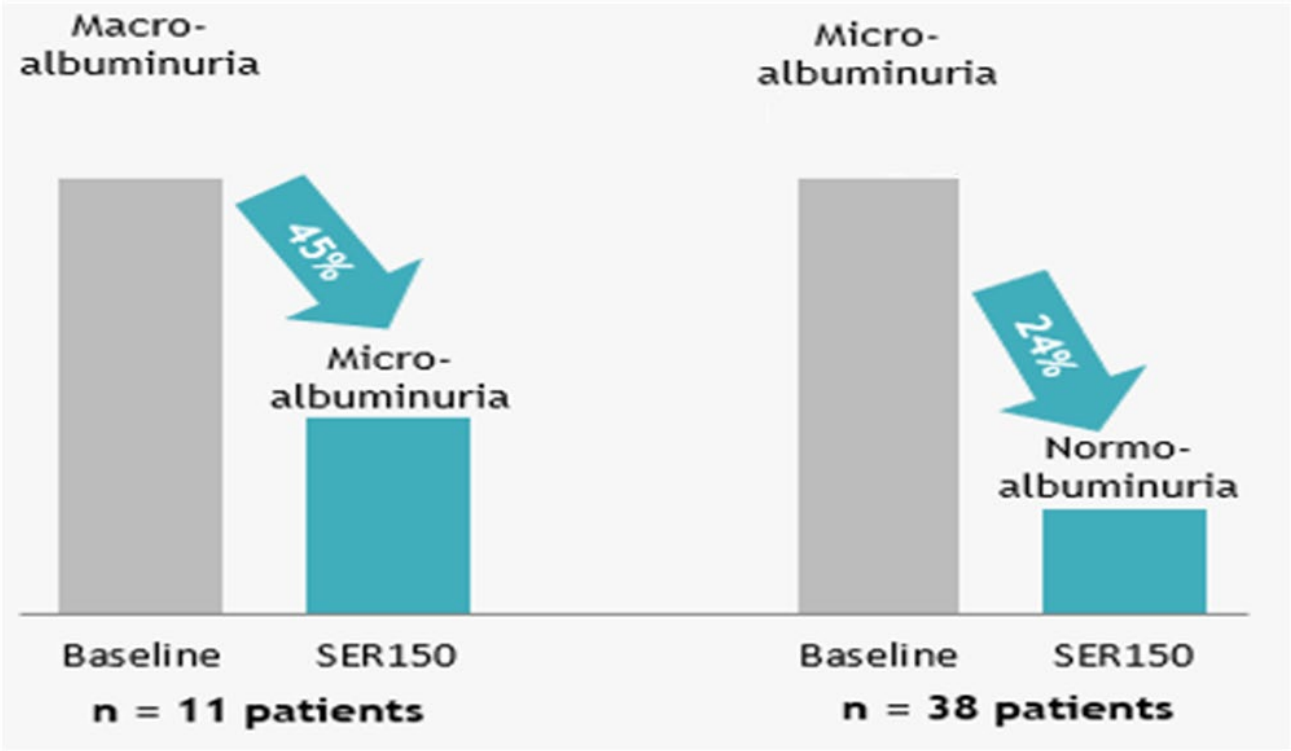
*ACR: Urine albumin corrected for creatinine

** BID: Bis in die (dosage taken twice daily)

SER150 – Clinical Proof of Concept

Induces remission in patients with Diabetic Kidney Disease

SER150 Dose 15 or 30 mg BID for 4 weeks, Phase 2 study results



>300 mg/g cr: Macroalbuminuria

≥ 30 < 300 mg/g cr: Microalbuminuria

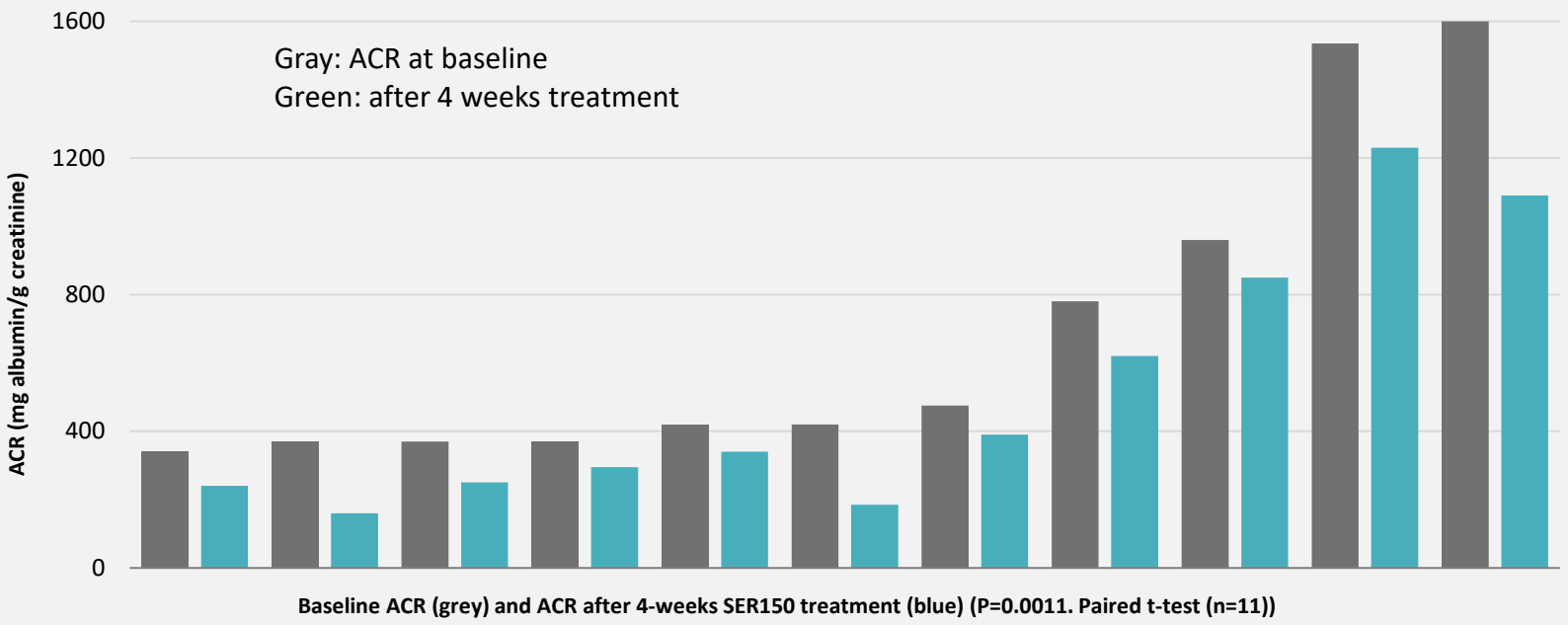
<30 mg/g cr: Normoalbuminuria

cr=creatinine

No safety or tolerance issues

SER150 study results (2/2)

Significant ACR reduction in all patients with macro-albuminuria



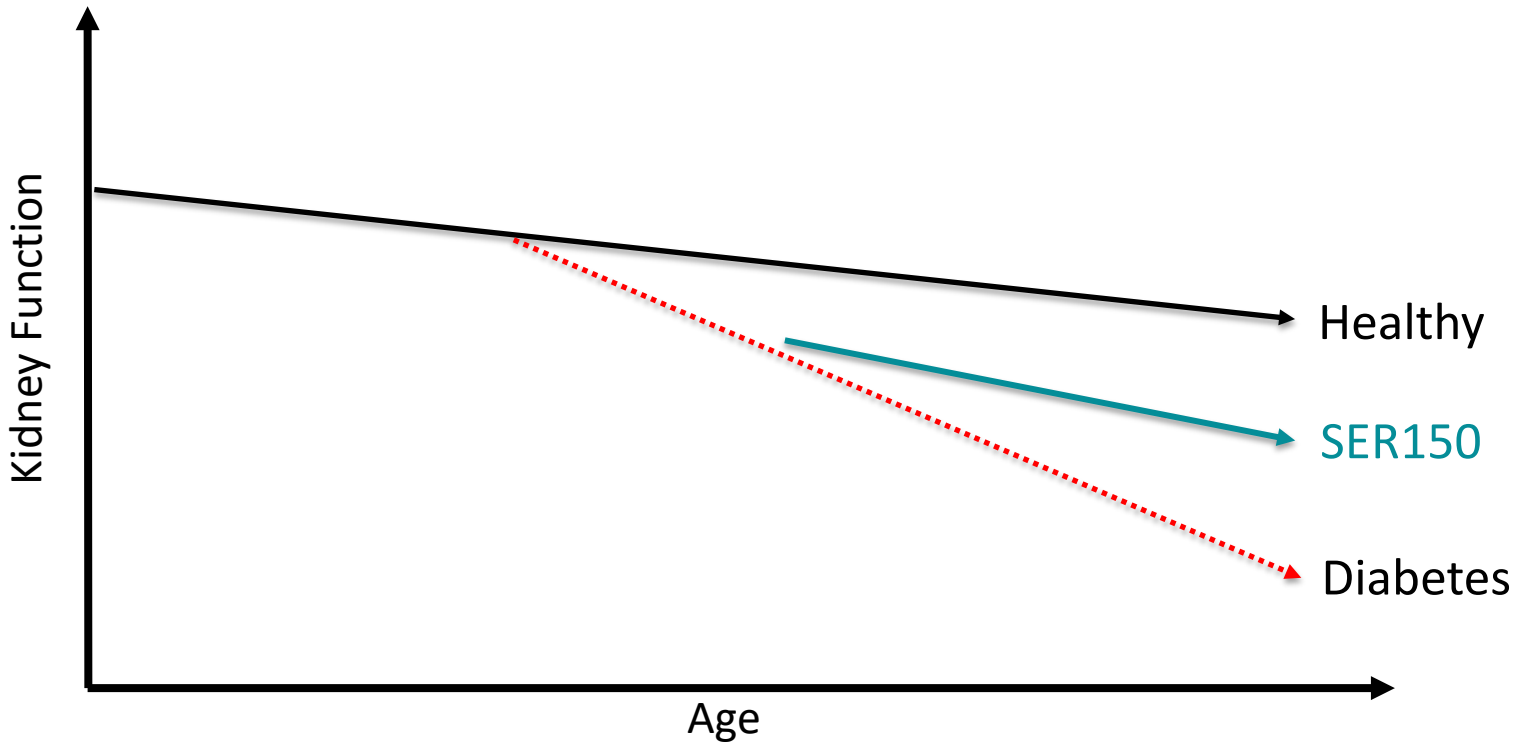
Baseline ACR (grey) and ACR after 4-weeks SER150 treatment (blue) (P=0.0011. Paired t-test (n=11))

- 22% of all SER150 treated patients had macro-albuminuria
- ACR decreased in all patients (P<0.001)
- No significant changes in macro-albuminuria during placebo treatment

Source: SER150 CLII-R007

Loss of Kidney Function in Healthy and Diabetics

Treatment with SER150 normalizes Kidney Function



Urinary albumin is a strong biomarker of Kidney Function

SER150 CL-009 Ongoing Clinical Study

Phase 2/3 – Placebo Controlled

Study SER150 CL-009, 6 months dosing, in Australia and New Zealand

Study inclusion criteria:

- Age 18-85, well controlled type 2 diabetes, HbA1c ≤ 10%
- In concomitant treatment with ACE inhibitor or ARB antagonist
- Macroalbuminuria (ACR >300 mg/g creatinine), no upper limit
- eGFR below 75 mL/minute/1.73 m^2 and above 15 mL/minute/1.73 m^2
- Blood pressure ≤ 160 mmHg systolic, and ≤ 100 mmHg diastolic
- Prothrombin within normal values

Primary endpoint:

Change of urine albumin-to-creatinine ratio (UACR) of > 30% from Baseline to Day 168

HbA1c = Hemoglobin A1c
ACE = Angiotensin-Converting Enzyme
ARB = Angiotensin Receptor Blocker
ACR = Urine Albumin to Creatinine Ratio
eGFR = Estimated Glomerular Filtration Rate

SER150 CL-009 Ongoing Clinical Study

Severity of included patient population

Patients with both Diabetes and Renal Involvement are three times more likely to die of Cardiovascular Disease

eGFR ml/min/1.73m²	Albuminuria categories Albumin:Creatinine ratio spot urine		
	A 1 <3 mg/mmol	A 2 3-30 mg/mmol	A 3 >30 mg/mmol
G1 ≥ 90	No CKD	G1 A2	G1 A3
G2 60-89	No CKD	G2 A2	G2 A3
G3a 45-59	G3a A1	G3a A2	G3a A3
G3b 30-44	G3b A1	G3b A2	G3b A3
G4 15-29	G4 A1	G4 A2	G4 A3
G5 <15	G5 A1	G5 A2	G5 A3

Increasing risk

Increasing risk

The patient population for SER150 ongoing Phase 2/3 study

ACR: mg/g conv. factor 0,11 to mg/mmol

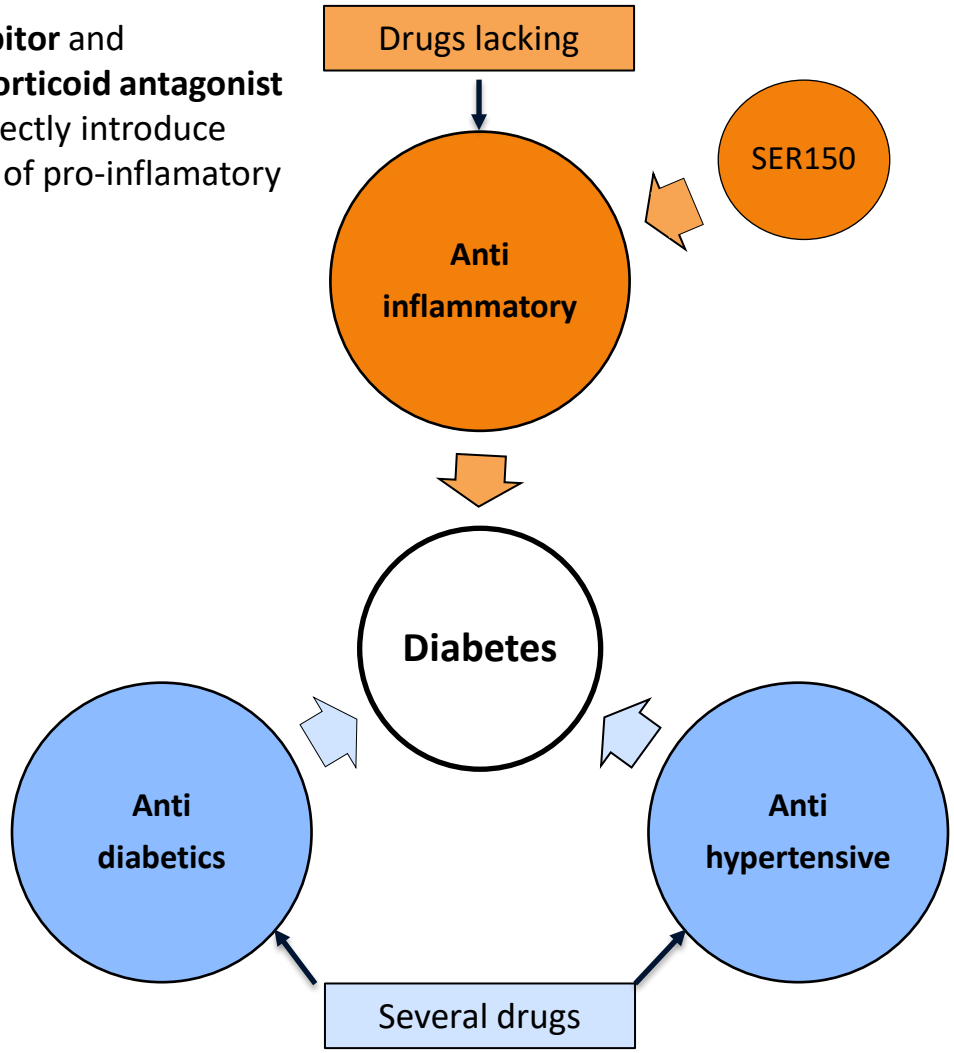
Source: National Kidney Foundation

What we know about

SER150

Diabetic Kidney Disease
Treatment Options

SGLT2inhibitor and **Mineralocorticoid antagonist** might indirectly introduce lower load of pro-inflamatory stress



SER150 inhibits directly and indirectly the low-grade inflammatory processes

Low dose Aspirin has

- an unpredictable effect on cardiovascular events in T2D patients
- limited effect on eGFR and/or ACR in patients with Diabetic Kidney Disease

Ref: Saito 2011. Okada 2015, Bell 2018, Barrera-Chimal, Vallon 202, Wu 2022

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SER150 Studies

Inhibits low-grade inflammation, halts progression of DKD

SER150 studied in subjects with Diabetic Kidney Disease

- SER150 CL-007
  - **Clinical Proof of Concept**, demonstrated in a Phase 2 placebo-controlled trial
  - Significant decreased urinary albumin in patients with diabetic kidney disease

- SER150 CL-009
  - Phase 2/3 trial, placebo-controlled study
  - **Ongoing** - recruiting patients with type 2 diabetes, high urinary albumin and reduced kidney function

- Other Clinical and Nonclinical studies
  - Before first study in patients with Diabetic Kidney Disease a number of SER150 single and multiple dose studies were performed in heathy volunteers and one study in patients with Type 2 Diabetes and normal kidney function

  - Large number of Pharmacological studies
  - All 9- and 6-months toxicological studies are reported in dog and rat
  - All safety pharmacological studies are reported

SER150 Nonclinical findings

Inhibits low-grade inflammation, halts progression of DKD

- Plasma half-life (steady state dosing) is ~9 hours
- No inhibition of CYP450 enzymes
- Metabolized mainly by CYP2C8
- No drug-drug interactions are expected

- Oral Administration

- Scalable drug substance synthesis
- Currently administered as minitablets in capsules
- Simplifying formulation is an option

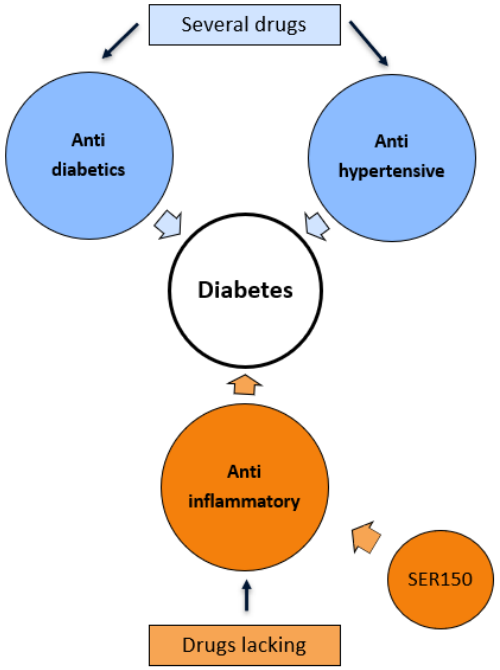
- SER150 patented for Treatment of renal diseases – protected to 2040

The Competitive situation

for

SER150

Competitive Market – Registered or Phase III drugs
Diabetic Kidney Disease

Compound	Company	Label	Treatment Options
SGLT2 inhibitor Approx 10 different drugs marketed from 2014-2019	Various Big Pharma companies world-wide	Antidiabetic drug for treatment of T2D Indication (Aug-2020): • Reduce risk Cardiovascular events • Reduce risk of End Stage Kidney Disease	
Mineralocortoid receptor antagonist	Bayer	Treatment of type 2 Diabetes, Indication (Feb-22): • Reduce the risk of sustained eGFR decline • Reduce risk of End Stage Kidney Disease, Cardiovascular death	
Mineralocortoid receptor antagonist	Daiichi Sankyo	Phase III, approved for treatment of Heart Failure	

Related drugs are marketed in non-DKD indications

- Bronica (Seratrodast), thromboxane receptor antagonist; Takeda, Asthma
- Plactidil (Picotamide), thromboxane synthase inhibitor and thromboxane receptor inhibitor; Teofarma, Peripheral artery disease

SGLT2 = Sodium-GLucose coTransporter-2
T2D = Type 2 Diabetes
eGFR = estimated Glomerular Filtration Rate

Serodus: Addressing unmet needs in Diabetic Kidney Disease

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