SERPIN PHARMA

SP16: Revolutionary Anti-Inflammatory Drug Platform

Transforming Anti-Inflammatory Therapy: A New Standard of Care

First-in-Class LRP1 Agonist · Patent-Protected to 2045 and beyond· Three Phase 2 Trials Q2 2026

Q2 2026 · NON-CONFIDENTIAL

Executive Summary — SP16 Platform Overview

SP16: First-in-Class LRP1 Agonist

A proprietary short peptide derived from Alpha-1 Antitrypsin (A1AT) that activates LRP1 — a master regulator of inflammation and cell repair. Controls disease-driving pathways without immunosuppression.

SP16's Unique Mechanism

- Controls critical disease-driving pathways
- Modulates harmful immune responses — without immunosuppression
- Promotes cellular and tissue repair simultaneously

Acute Myocardial Infarction

Reperfusion Injury

- Phase 2 planned Q2 2026
- POC data in STEMI

Acute Kidney Injury

Cardiac Surgery Associated

- Phase 2 planned Q2 2026
- Renal protection focused

Cancer Pain (CIPN)

Chemo-Induced Neuropathy

- Licensed to Dogwood Therapeutics
- Phase 1b funded by NCI

Platform Expansion

Oral Analogs + Metabolic

- CKD, Heart Failure, Obesity
- Diabetes — extending to chronic disease

Strategic Partnerships

Estée Lauder (exclusive skincare license) · Dogwood Therapeutics (CIPN license) · FAU Erlangen, Sheba Medical, MetroDerm (clinical partners)

Competitive Strengths

Strong patent estate through 2042 · Experienced leadership & scientific advisory board · Active collaborations across therapeutic and consumer health

Partnering Opportunity

Actively seeking global and regional partners to expand SP16's reach across inflammation-driven diseases · Phase 2 launching Q2 2026

The Problem: The Immunosuppression Trap

The Immuno-suppression Trap

Current steroids and biologics often disable the immune system — leaving patients vulnerable to infection, opportunistic disease, and poor long-term outcomes.

SP16 — A Completely New Approach

The Solution

SP16 — a synthetic 17 amino acid peptide derived from Alpha-1 Antitrypsin that activates LRP1, a master regulator of immune homeostasis.

Dual Action Mechanism

Simultaneously inhibits pro-inflammatory NFκB signaling while activating Akt/ERK repair pathways — reducing harmful mediators while promoting healing.

Non-Immunosuppressive

Rebalances immune responses while preserving the body's natural ability to fight infection. No immunosuppression, no immunogenicity risk.

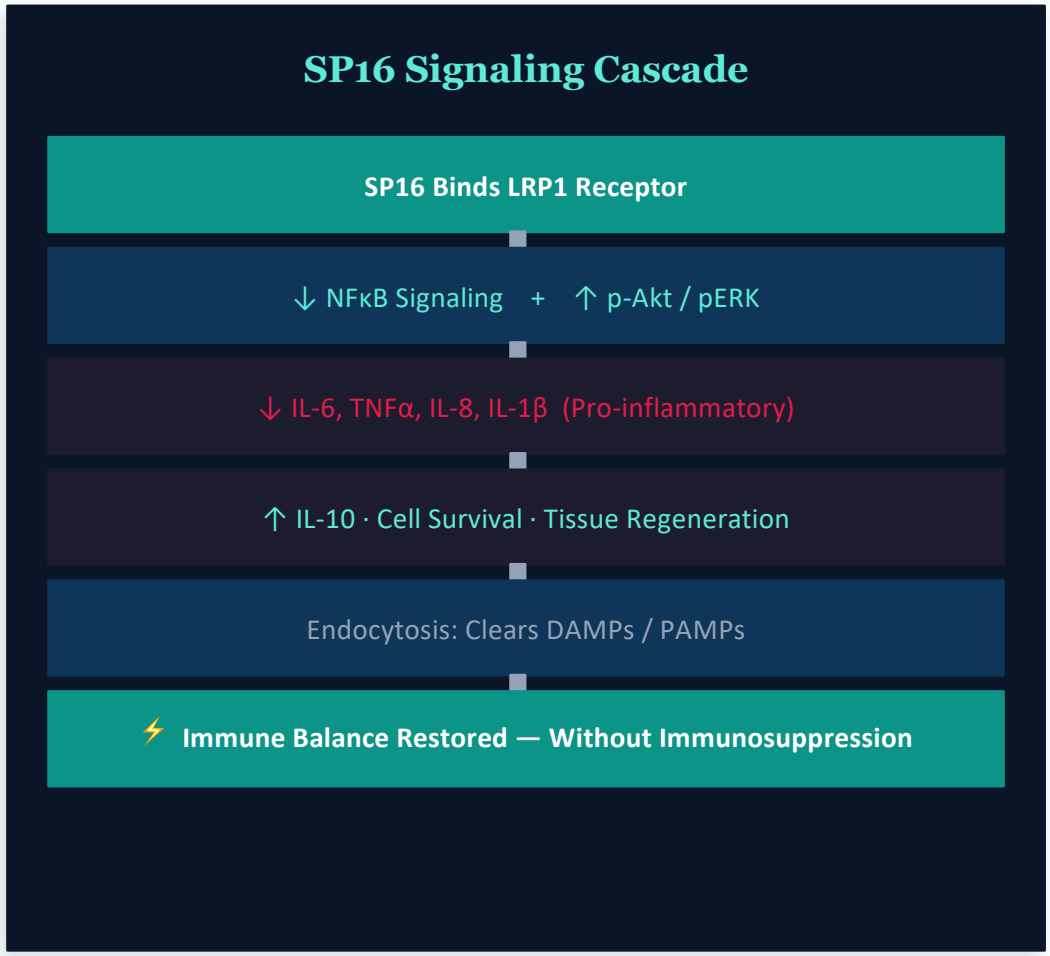
Universal Platform

SP16 is cell-type agnostic and injury-type agnostic — the same molecule works across AMI, AKI, neuropathic pain, skin disease, obesity, and more.

Mechanism of Action — LRP1 Agonism

SP16 is a Potent LRP1 Agonist

- LRP1 (LDL-receptor related protein-1) is a signaling and endocytic receptor critical in controlling the immune response
- Expressed on virtually all cell types — making SP16 cell-agnostic and injury-agnostic
- SP16 is the world's first-in-class LRP1 agonist — no other approved therapy targets this pathway
- Endocytic function clears DAMPs/PAMPs from the cell environment — upstream inflammasome regulation
- Reduces harmful inflammatory mediators (IL-6, TNFα, IL-8, IL-1β) while increasing resolving mediators (IL-10)



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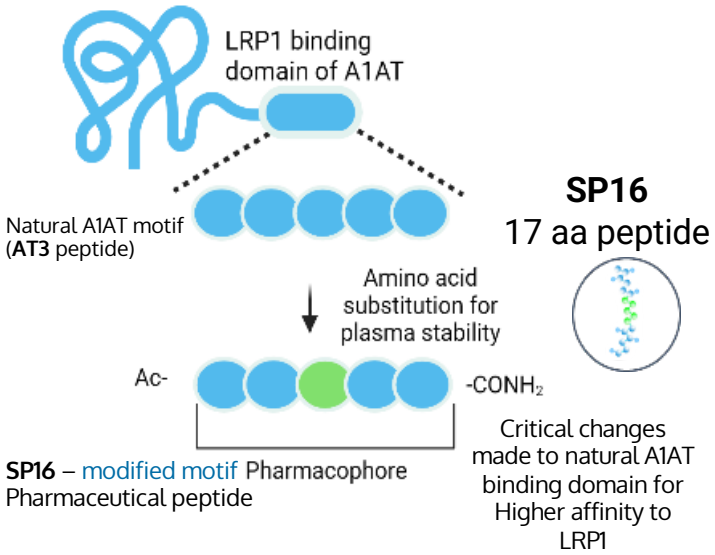
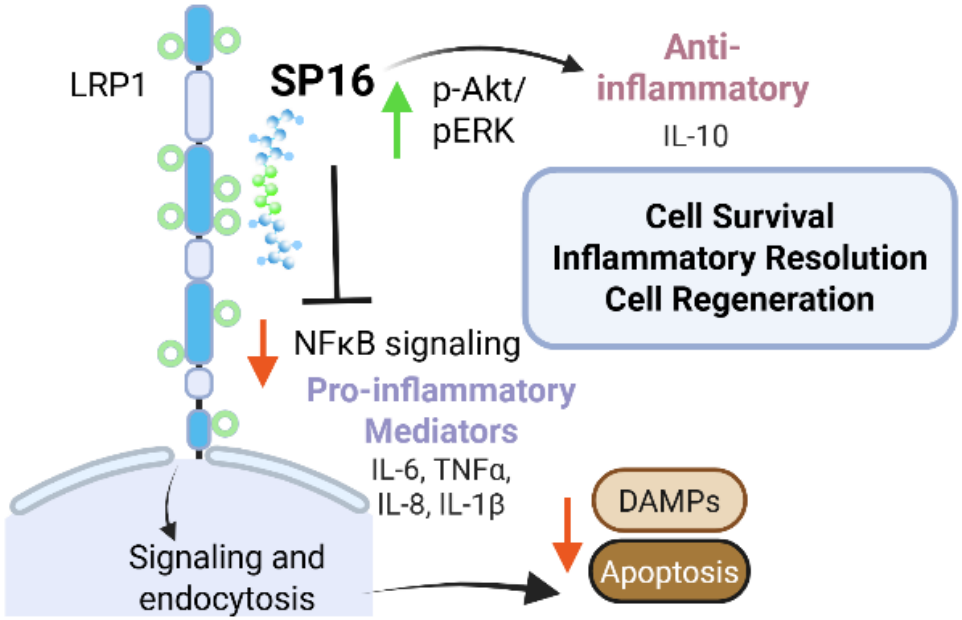
Discovery of SP16 as a Breakthrough in LRP1 agonism to safely target a root cause of inflammatory diseases

SP16 is a safe and natural solution to inflammatory disease



InhibRX (developing an A1AT recombinant) was acquired in 2024 by Sanofi for $2.2 B

SP16's non-immunosuppressive mechanism maintains the body's natural ability to heal during inflammation



SP16 PLATFORM

$50B – $80B+

Annual market opportunity across all acute, chronic & new indications

ACUTE & CHRONIC INDICATIONS (existing)

$9.7B
Acute kidney injury
No approved therapy exists

$9B
Heart failure
Chronic inflammation driver

$8B+
Chronic kidney disease
Massive global prevalence

$0.6B
Acute myocardial infarction
Acute cardioprotection

AUTOIMMUNE & SYSTEMIC — ORAL

NEW

$30B+
Rheumatoid arthritis
Oral SP16 analog; systemic inflammation

$4B+
Lupus (SLE)
Oral SP16 analog; immune dysregulation

$22B+
Multiple sclerosis
Oral SP16 analog; neuroinflammation

DERMATOLOGY — TOPICAL / ORAL

NEW

$40B+
Psoriasis
Topical & oral SP16; inflammatory skin plaques

ALLERGY / HYPERSENSITIVITY — INHALED / ORAL / TOPICAL

NEW

$22B+
Asthma
Type 2 & non-type 2 airway inflammation

$5B+
Eosinophilic esophagitis
Validated in Rothenberg/Cincinnati data

$13B+
Eczema (atopic dermatitis)
Topical & systemic; allergic inflammation

MUSCULOSKELETAL — INTRA-ARTICULAR INJECTION

$15B+
Osteoarthritis
Intra-articular SP16; synovial inflammation & cartilage repair

mRNA-encoded SP16 patents also filed for chronic joint inflammation — enabling sustained intra-articular delivery without repeated injections

SP16 = pipeline-within-a-product across acute, chronic & new indications

$50B – $80B+ TAM

SP16 Wins Every Comparison

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🏆 **InhibRx acquired by Sanofi for $2.2B (2024) — same target**

Feature	SP16 Platform	Plasma-Derived A1AT	Recombinant A1AT-Fc (InhibRx)
Potency	**300x higher than natural A1AT**	Standard / compromised structure	Complex size & structure
Administration	**Self-injected SC + oral/topical/mucosal (in development)**	1–2 hour clinic infusion	1–2 hour infusion only
Administration Time	**Instantaneous (subcutaneous injection)**	Long (1–2 hours in clinic)	1–2 hours
Supply / COGS	**Unlimited synthetic supply, low cost**	Scarce — extracted from plasma	High complexity; yield TBD
Safety	**No immunosuppression risk**	Risks from plasma-derived products	Immunogenicity (Fc portion)
IP Position	**Patented through 2042**	Off patent	Patented
Mfg. Complexity	**Low**	High	High

A Broad & De-Risked Pipeline

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PROGRAM	INDICATION	FORMAT	STAGE	PARTNER
SP16	**Acute Kidney Injury (AKI)**	Injectable Peptide	PHASE 2	*FAU Erlangen-Nürnberg*
SP16	**Acute Myocardial Infarction (AMI)**	Injectable Peptide	PHASE 2	*BIRD / Sheba Medical Center*
SP16	**Cancer Pain — CIPN**	Injectable (IV)	LICENSED	*Dogwood Therapeutics + NCI*
SP16	**Severe Skin Disease**	Topical / Injectable	PHASE 2 READY	*MetroDerm*
RL-Series	**CKD, Heart Failure**	Oral Cyclic Peptide Analogs	PRECLINICAL	*Open for Partnering*
AT3	**Skincare / Anti-Aging**	Natural Peptide	LICENSED	*Estée Lauder Companies*

Proof of Concept Already In Hand

Phase 1 — Healthy Volunteers

Published in PLOS ONE (2021) — First-in-Class LRP1 Agonist

- Safe and well-tolerated at all dose levels tested
- No serious adverse events reported at any dose
- Favorable pharmacokinetic profile established
- Dose-dependent plasma exposure confirmed

✓ **Cleared — Phase 2 Ready Across Multiple Indications**

Phase 2 — STEMI / AMI Trial

n=10 SP16 vs. n=28 historical placebo control

- Significantly lowered CRP (inflammatory marker, p=0.0147)
- Reduced CK-MB — surrogate marker for infarct size
- Preserved left ventricular ejection fraction at 1-year follow-up
- Significant reduction in heart failure events vs. placebo

0%	26%
SP16 Hospitalization Rate	Placebo Hospitalization Rate

SP16 Prevents Diet-Induced Cardiac Dysfunction (HFpEF/HFrEF)

In collaboration with Drs. Antonio Abbate and Stefano Toldo (VCU Health) — SP16 demonstrated strong cardioprotection in obese mouse models.

Study Design

- Western Diet (high fat/sugar) for 4 weeks → glucose intolerance & obesity
- Then 4 additional weeks: WD alone, WD + SP16 (4µg/mouse), or WD + scrambled control (SP34)
- Endpoints: body weight, fasting glucose, oral glucose tolerance, echocardiography
- AMI induced: infarct size measured after 30 min ischemia + 24h reperfusion

Cardiac Function Rescued

SP16 reversed obesity-induced worsening of ejection fraction, myocardial performance index, and isovolumetric relaxation time. Scrambled control (SP34) was ineffective.

Infarct Size Reduced

Chronic low-dose SP16 significantly reduced infarct size in obese mice. Acute high-dose SP16 at reperfusion also effective. SP34 showed no protective effect.

HFpEF & HFrEF Relevance

Addresses unmet need where current therapies show limited benefit. SP16's dual anti-inflammatory + regenerative mechanism uniquely targets both HFpEF and HFrEF populations.

Key Insight: LRP1 agonists uniquely target both inflammation and tissue repair — positioning SP16 as a novel therapy for HFpEF and HFrEF populations.

EMERGING OPPORTUNITY

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SP16 in Obesity & Metabolic Disease

Boehringer Ingelheim scientists independently validated SP16 as a novel GIP receptor agonist with broad metabolic benefits — opening an entirely new strategic dimension for the platform.

Novel GIPR Agonist

SP16 drives lipolysis via cAMP in human adipocytes, increasing free fatty acids. Boosts mitochondrial oxygen consumption via β-oxidation, improving energy expenditure.

Proven in Obese Mice

A single SC dose of SP16 in diet-induced obese (DIO) mice improved glucose clearance dose-dependently. Significantly reduced glucose AUC, elevated FFAs, and reduced leptin.

Complements GLP-1

While GLP-1/GIP drugs suppress appetite, SP16 restores adipocyte metabolic function and reduces chronic adipose inflammation — a differentiated, synergistic mechanism.

Dual Pathway Action

Targets both metabolic inflexibility (cAMP↑, lipolysis↑, glucose tolerance↑) AND chronic adipose inflammation via LRP1-mediated resolution signaling.

bioRxiv 2025 — Boehringer Ingelheim Research · doi:10.1101/2025.06.17.660082

Alpha-1-Antitrypsin Deficiency (AATD) — An Emerging Indication

AATD is a genetic disorder where a nonfunctional, toxic variant of A1AT accumulates in the liver — causing cell damage and loss of lung-protective function. Over 40% of AATD patients develop COPD.

The Problem in AATD

A1AT is not produced in sufficient amounts, resulting in unchecked neutrophil elastase (NE) activity. This drives chronic inflammation, tissue damage, and loss of lung function.

SP16 Does NOT Need Protease Activity

SP16 and LRP1-derived analogs don't retain A1AT's protease-inhibitor activity — but are far more potent anti-inflammatory molecules via direct LRP1 agonism.

Preclinical Data Confirms

In OVA-challenged mice and human esophageal epithelial cells, SP16 and LRP1 agonist peptides significantly reduced inflammatory cytokines (TSLP, IL-1α) — protease inhibition not required.

Oral Delivery Advantage

Oral LRP1 agonist dosage forms are in development, avoiding the invasive weekly IV infusions required by current A1AT replacement therapies (Baxter, Grifols, CSL Behring).

	A1AT Replacement Therapy	LRP1 Agonist (SP16)
Route	Intravenous (weekly–monthly)	Oral (daily) — in development
LRP1-Binding	Indirect (NE:A1AT complex)	Direct — far more potent
Inflammation	↓ (modest)	↓↓↓ (highly potent)
Tissue Repair	↑ (limited)	↑↑↑ (strong regenerative effect)

RL-Series: Next-Generation Orally Available Analogs

Optimized design for chronic disease — shorter peptides retaining the active LRP1-binding pharmacophore with improved potency, stability, and oral bioavailability.

20–50x Increased Potency

SP16 analogs show dramatically improved NFκB inhibition in reporter assays. Best analogs (RL5B, RL2-5) have IC50 of 1.17–1.46 µg/mL vs SP16 at 47.1 µg/mL.

Oral Bioavailability ≥7%

Lead cyclic and linear analogs demonstrate oral bioavailability exceeding bioactivity thresholds — enabling daily oral dosing for chronic indications.

Zero Toxicity

A1AT-derived analogs mimic SP16's anti-inflammatory activity across monocytic and microglial cells with no cytotoxicity at tested concentrations.

Format Flexibility

Short 8–10 mer peptides maintain the precise LRP1 pharmacophore. Improved solubility enables broad formulation options: oral, topical, injectable.

Selected Analog IC50 Comparison (NFκB inhibition — lower = more potent)

Marquee Partners Validate the Platform

Partnerships provide external validation of the technology, non-dilutive capital to fund clinical programs, and proven operational expertise.

EXCLUSIVE LICENSE

Estée Lauder

Consumer Health · Exclusive License

Exclusive partnership to develop anti-aging and regenerative skincare using Serpin's natural AT3 peptide portfolio. Serpin received an upfront cash payment plus eligibility for future milestone payments.

LICENSED + NCI FUNDED

Dogwood Therapeutics

Therapeutics · Licensed Program + NCI Funded

Full upfront payment in unrestricted DWTX stock for SP16 IV license in chemotherapy-induced peripheral neuropathy (CIPN). Phase 1b funded by NCI launching Q2 2026. Dogwood brings proven regulatory and clinical execution track record.

4 ACTIVE TRIALS

Academic & Clinical Network

4 Active Trial Partners

FAU Erlangen-Nürnberg (AKI Phase 2) · Sheba Medical Center (AMI Phase 2) · MetroDerm (Skin Phase 2a) · University of Virginia · Yale University · UC San Diego · Cincinnati Children's · Virginia Tech

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Strategic partnerships generate non-dilutive capital while providing independent validation of SP16's therapeutic and commercial potential.

Fortified Intellectual Property Portfolio

13	16	5	2042
Patents Issued	Total Applications	Patent Families	Longest Patent Life

SP16 (AT3) — Natural Sequence | Filed 2011 & 2022

Foundation patents on the natural A1AT amino acid motif (AT3 peptide) and its anti-inflammatory uses. Wholly owned by Serpin Pharma.

SP16-3M — Modified LRP1 Agonist | First expiry: 2035

Core pharmaceutical asset with enhanced LRP1 affinity modifications. The proprietary drug platform — higher potency (300x) vs natural A1AT.

RL-Series — Next-Gen Oral Analogs | First expiry: 2042

Shorter cyclic and linear peptide analogs with extensive modifications outside the binding motif. Oral bioavailability ≥7%; 20–50x potency increase.

mRNA-Encoded SP16 | Expansion

Long-lasting SP16 expression for osteoarthritis and other chronic inflammatory conditions. Enables sustained treatment without repeated injections.

SP16 Wound Dressings & Topicals | Expansion

SP16-impregnated patches, films, and wound dressings for dermatological and wound healing applications. Partnered with MetroDerm for skin diseases.

World-Class Leadership Team

Proven track record in anti-inflammatory drug development. Scientific advisors from Stanford, Cincinnati Children's, Yale, Johns Hopkins, and more.

Cohava Gelber
PhD, MBA

Founder, President & CEO

Larry Altstiel
MD, PhD

Acting CMO & SAB Member

Dana Austin
PhD

VP Research & Development

Mark Spear
PhD

VP Discovery Research

Amit Hyzjyhu

VP Pharmaceutical Engineering

Dan Aitkens
CPA

Acting CFO

Cohava Gelber, PhD MBA (CEO) · Denise Barbut, MD (Cornell University) · Alexander (Zan) Fleming, MD (FDA, Kinexum) · Lawrence Steinman, MD (Stanford) · William B. Johns, MBA (Healthcare Capital Corp.)

Scientific Advisory Board: Antonio Gotto (Weill Cornell) · Lawrence Steinman (Stanford) · Marc Rothenberg (Cincinnati Children's) · Wendy Campana (UC San Diego) · Jack Arbiser (Emory/MetroDerm) · Jonathan Zenilman (Johns Hopkins) · Jerome Zeldis · Alexander (Zan) Fleming · Gordon Smith (VCU)

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Serpin Pharma is defining the Future of Inflammation

Serpin is positioned as a platform-level leader in inflammation-driven and metabolic disease.

Cohava Gelber, PhD, MBA
CEO & Chairperson of the Board

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Platform Highlights

First-in-Class

Only LRP1 agonist — no approved competing therapy exists

$17B–$30B+ TAM

Across AKI, Heart Failure, CKD, AMI, Obesity, AATD

De-Risked

Phase 1 complete · 2 Phase 2 launching Q2 2026

Validated

Estée Lauder · Dogwood · Boehringer Ingelheim · NIH

Protected

13 issued patents across 5 families through 2042

Scalable

Synthetic peptide — unlimited supply at low COGS

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Additional Information

Serpin is positioned as a platform-level leader in inflammation-driven and metabolic disease.

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Therapeutic activity of SP16 has been demonstrated across multiple disease models by independent researchers at premier institutions

Inflammation is at the core of many different diseases

SP16 targets natural pathways of inflammatory diseases

SP16 is agnostic to injury or cell type making it a universal solution

The scientific basis of SP16 activity is strong

AMI (ischemia/ reperfusion injury)

Antonio Abbate, MD, PhD

University of Virginia

Peripheral Nerve Injury/Pain

Wendy Campana, PhD

UC San Diego

Eosinophilic Esophagitis, AD (Allergic

Marc Rothenberg MD, PhD
Nurit Azouz, PhD

Cincinnati Children's

Lung Injury (ARDS/COVID-19)

Michael Shim, MD

University of Virginia

Kidney Disease (Proteinuric)

Shute Ishibe, MD

Yale University

Kidney Disease (Ischemic)

Tilman Jobst-Schwan, MD

Uniklinikum Erlangen

Neuroinflammation HIV Brain Infection

Nazira El-Hage, PhD

FIU Florida International University

Infectious Disease, Encephalitic Virus

Kylene Kehn-Hall, PhD

Virginia Tech

Published Manuscripts Covering Serpin's Technology

LOW-DENSITY LIPOPROTEIN RECEPTOR–RELATED PROTEIN-1 IS A THERAPEUTIC TARGET IN ACUTE MYOCARDIAL INFARCTION – JACC BASIC TRANSL SCI 2017 OCT 30;2(5):561-574. DOI: 10.1016/J.JACBTS.2017.05.007SCIENCEDIRECT
OCTOBER 2017

FRONTIERS | LOW DENSITY LIPOPROTEIN RECEPTOR-RELATED PROTEIN-1 IN CARDIAC INFLAMMATION AND INFARCT HEALING | CARDIOVASCULAR MEDICINE (FRONTIERSIN.ORG) (HTTPS://WWW.FRONTIERSIN.ORG/ARTICLES/10.3389/FCVM.2019.00051/FULL)
APRIL 2019

A PHASE 1 CLINICAL TRIAL OF SP16, A FIRST-IN-CLASS ANTI-INFLAMMATORY LRP1 AGONIST, IN HEALTHY VOLUNTEERS (PLOS.ORG) (HTTPS://JOURNALS.PLOS.ORG/PLOSONE/ARTICLE?ID=10.1371/JOURNAL.PONE.0247357) MAY 2021

A1-ANTITRYPSIN DERIVED SP16 PEPTIDE DEMONSTRATES EFFICACY IN RODENT MODELS OF ACUTE AND NEUROPATHIC PAIN (WILEY.COM) (HTTPS://FASEB.ONLINELIBRARY.WILEY.COM/DOI/EPDF/10.1096/FJ.202101031RR)
NOVEMBER 2022

SAFETY, TOLERABILITY AND EFFECTS OF A SINGLE SUBCUTANEOUS AD... : JOURNAL OF CARDIOVASCULAR PHARMACOLOGY (LWW.COM) (HTTPS://JOURNALS.LWW.COM/CARDIOVASCULARPHARM/ABSTRACT/9900/SAFETY,_TOLERABILITY_AND_EFFECTS_OF_A_SINGLE.79.ASPX)
JULY 2022

ANTI-INFLAMMATORY THERAPY FOR ACUTE CORONARY SYNDROMES: IS I... : JOURNAL OF CARDIOVASCULAR PHARMACOLOGY (LWW.COM) (HTTPS://JOURNALS.LWW.COM/CARDIOVASCULARPHARM/CITATION/9900/ANTI_INFLAMMATORY_THERAPY_FOR_ACUTE_CORONARY.85.ASPX)
JULY 2022

SERPIN-DERIVED SMALL PEPTIDE (SP16) AS A POTENTIAL THERAPEUTIC AGENT AGAINST HIV-INDUCED INFLAMMATORY MOLECULES AND VIRAL REPLICATION IN CELLS OF THE CENTRAL NERVOUS SYSTEM. CELLS (HTTPS://WWW.MDPI.COM/2139508) FEBRUARY 2023