

Semnur Pharmaceuticals

Getting Back to Normal

Corporate Presentation (OTC: SMNR)

Semnur Pharmaceuticals™

Majority Owned Subsidiary of Scilex Holding Company (NASDAQ: SCLX)

SP-102 (SEMDEXA) Opportunity

Semnur Pharmaceuticals™
Getting Back to Normal

- Market Opportunity
- Unmet needs
- Product Profile
- Clinical Development
- Reimbursement
- Sales Forecast

Safe Harbor Statements Forward-Looking Statements

Semnur Pharmaceuticals™
Getting Back to Normal

Certain statements contained in this corporate presentation (this "Presentation"), along with certain statements that may be made by management of Semnur Pharmaceuticals ("Semnur") orally in presenting this material, are or may be considered "forward-looking statements". These statements can be identified by the fact that they do not relate strictly to historic or current facts. Forward-looking statements are typically identified by words such as "estimate," "expect," "intend," "believe," "plan," "anticipate," "potential," "projected" and other words and terms of similar meaning (including the negative of any of the foregoing) in connection with any discussion of future operating or financial performance or condition, but the absence of these words does not mean that a statement is not forward-looking. In addition, any statements that refer to projections, forecasts, or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. Semnur cautions that these statements are based upon information available as of the date of this Presentation and the current beliefs and expectations of Semnur's management and are subject to significant risks, uncertainties and assumptions, and involve a number of judgements. Statements regarding future actions, future performance and/or future results including, without limitation, those relating to the timing for completion, and results of, scheduled or additional clinical trials and the FDA's or other regulatory review and/or approval and commercial launch and sales results (if any) of Semnur's formulations and product candidate and regulatory filings related to the same, financial projections and targets, business strategy and plans and objectives for future operations may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Presentation are inherently uncertain and may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, you should not rely upon forward-looking statements as predictions of future events.

Semnur undertakes no obligation to update publicly or revise any forward-looking statements for any reason after the date of this Presentation or to conform these statements to actual results or to changes in Semnur's expectations, whether as a result of new information, future events, inaccuracies that become apparent after the date hereof or otherwise, except as may be required under applicable securities laws.

Industry and Market Data

Certain data in this Presentation was obtained from various external sources, and neither Semnur nor its affiliates, advisers or representatives has verified such data with independent sources. Accordingly, neither Semnur nor any of its affiliates, advisers or representatives makes any representations as to the accuracy or completeness of that data or undertakes any obligation to update such data after the date of this Presentation. Such data involves risks and uncertainties and is subject to change based on various factors.

Trademarks

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Solely for convenience, trademarks, trade names and service marks referred to in this Presentation may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that the applicable licensor will not assert, to the fullest extent under applicable law, its rights to these trademarks and trade names. Such use should not be construed as an endorsement of the products or services of Semnur.

Important Information and Where to Find It

This Presentation does not constitute an offer to sell or exchange, or the solicitation of an offer to buy or exchange, any securities, nor shall there be any sale of securities in any jurisdiction in which such offer, sale or exchange would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. In connection with the proposed business combination with Denali Capital Acquisition Corp. ("Denali"), as more fully described elsewhere in this Presentation, Denali intends to file a Registration Statement on Form S-4 (the "Registration Statement"), which will include a document that serves as a prospectus and proxy statement of Denali, referred to as the proxy statement/prospectus.

Safe Harbor Statements Forward-Looking Statements

Semnur Pharmaceuticals™
Getting Back to Normal

After the Registration Statement is declared effective by the SEC, the proxy statement/prospectus will be sent to all Denali shareholders as of a record date for the meeting of Denali shareholders to be established for voting on the proposed business combination. Denali will also file other documents regarding the proposed transaction with the SEC. This Presentation does not contain all of the information that will be contained in the proxy statement/prospectus or other documents filed or to be filed with the SEC. Investors and securityholders of Denali are urged to read these materials (including any amendments or supplements thereto) and any other relevant documents in connection with the transaction that Denali files with the SEC when, and if, they become available because they will contain important information about Denali, Semnur and the proposed transaction. Investors and security holders will be able to obtain free copies of the Registration Statement, the proxy statement/prospectus and all other relevant documents filed or that will be filed with the SEC by Denali through the website maintained by the SEC at www.sec.gov.

Participants in the Solicitation
Denali and its directors and executive officers may be deemed participants in the solicitation of proxies from Denali's shareholders in connection with the transaction. A list of the names of such directors and executive officers and information regarding their interests in the proposed business combination will be contained in the proxy statement/prospectus when available. You may obtain free copies of these documents as described in the preceding paragraph. Semnur and its directors and executive officers may also be deemed to be participants in the solicitation of proxies from the shareholders of Denali in connection with the proposed transaction. Information about Semnur's directors and executive officers and information regarding their interests in the proposed transaction will be included in the proxy statement/prospectus for the proposed transaction.

Non-Solicitation
This Presentation is not a proxy statement or solicitation of a proxy, consent or authorization with respect to any securities or in respect of the potential transaction and shall not constitute an offer to sell or a solicitation of an offer to buy the securities of Denali, Semnur the combined company, nor shall there be any sale of any such securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of such state or jurisdiction. No offer of securities shall be made except by means of a prospectus meeting the requirements of the Securities Act of 1933, as amended.

SP-102 (SEMDEXA) Market Opportunity

Semnur Pharmaceuticals™
Getting Back to Normal



Developing SP-102 as a non-opioid injectable therapeutic for sciatica

Novel viscous gel formulation, optimized for epidural injection
Novel biocompatible excipient enables extended local effect



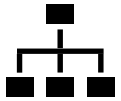
On track to be the first FDA-approved epidural steroid product for sciatica

Currently used products are off-label and contain potentially neurotoxic preservatives, particulates, surfactants or solvents. Compounded epidural steroids led to >70 deaths in 2012 due to fungal contamination



Large market over 12 million epidural steroid injections per year in U.S.

Bigger opportunity than knee intra-articular OA injections, with no direct competition Established reimbursement route for the most frequently performed pain procedure



Phase 3 CLEAR trial completed

Fast Track status granted by FDA



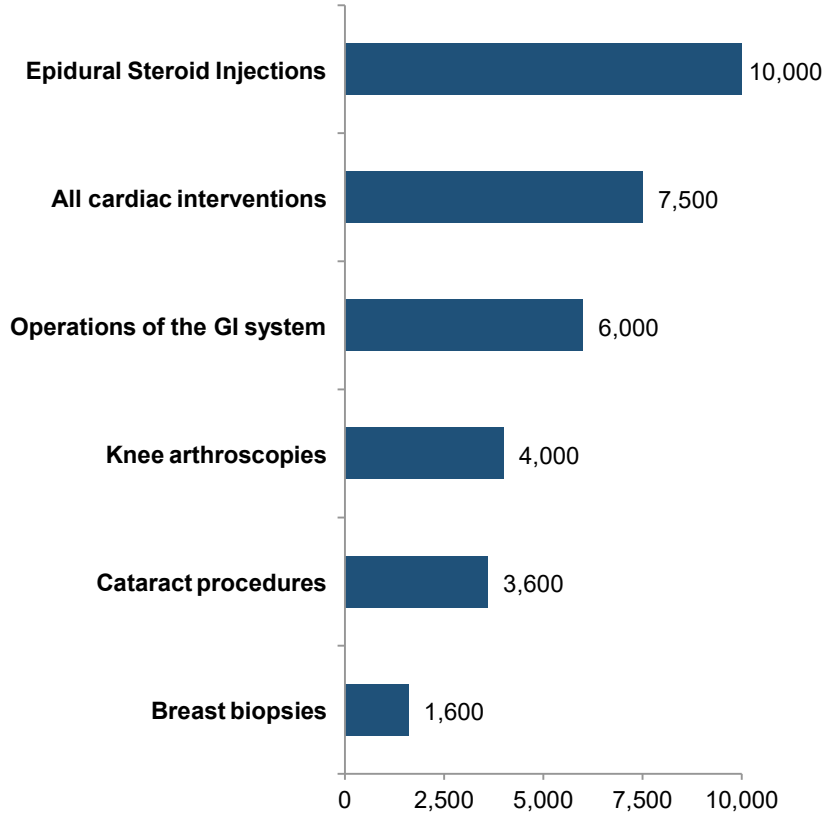
Strong proprietary platform with issued IP and high barriers to entry for competitors or generics

Method of use patent granted and formulation patent approved. Complex manufacturing process and know-how for excipient and sterile viscous gel products

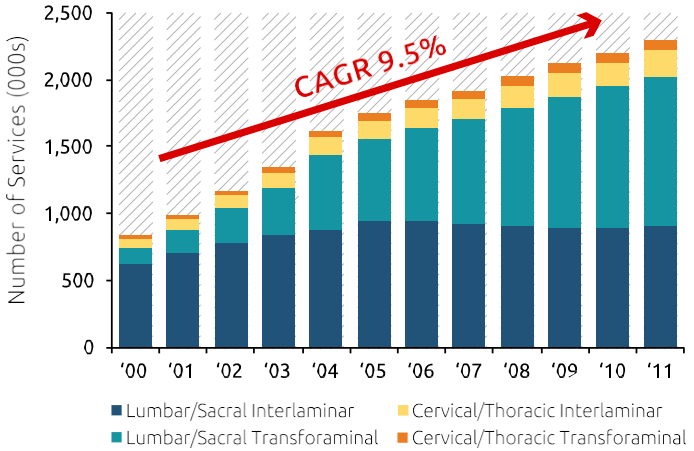
Epidural Steroid Injections Are One of the Most Common Medical Procedures in the U.S.

Semnur Pharmaceuticals™
Getting Back to Normal

Common Surgical Procedures (thousands) (1)



Strong Growth Rate, Evidenced by Medicare Procedure Volumes



Medicare Overall ESI Injection Volume (2)

- ESIs widely reimbursed as procedure to delay or avoid back surgery
- Transforaminal ESI route (used in Semnur CLEAR trial) majority of procedures

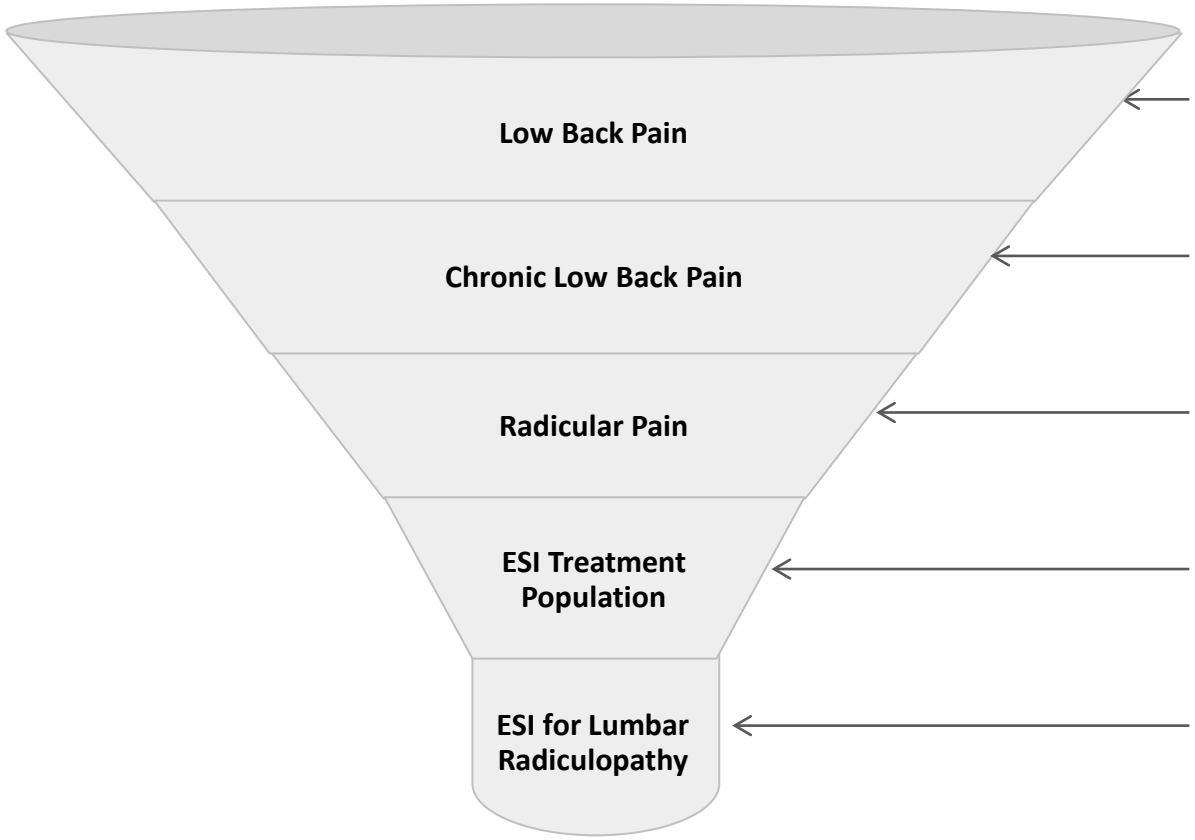
(1) CDC, HCUP, Semnur data on file.
(2) http://updates.pain-to pics.org/2012/01/epidural-steroid-injections.html, Accessed: ASIPP Conference 2012. Manchikanti. Medicare Slides.

SP-102 (SEMDEXA) Epidemiology—Overview

Semnur Pharmaceuticals™
Getting Back to Normal

Lumbar Radiculopathy is a subtype of Low Back Pain characterized by debilitating pain usually requiring medical intervention.

Treatment Funnel for ESI Treatment of Lumbar Radiculopathy



- ~80% of Americans will experience low back pain in their lifetime (~250 million)[1]
- Leading cause of disability in Americans

- Estimated ~26.0M US patients with chronic low back pain in 2022[2]
- Consists of back pain present for longer than 3 months

- Comprises of nerve pain in the neck, arms, legs, buttocks, and feet
- Patient, Physician collaborate to determine treatment decision
- Treat with **ESI**, Physical Therapy, Surgery or Opioids

- Estimated 11.2 M patients treated with ESIs in 2022[2]
- 2014-2018 CAGR was 0.5% for LR ESIs

- 88% of ESI procedures are used to treat Lumbar Radiculopathy
- Patients receive ~1.6 injections per year on average

Source: 1. Snarr, J Risks, Benefits, and Complications from Epidural Steroid Injections: A Case Report. June, 2007. Reinberg, S., 1 in 4 American Workers Struggles With Back Pain, https://www.webmd.com/back-pain/news/20190513/1-in-4-american-workers-struggles-with-back-pain#1 ; 2. Refer to slide 5-9

SP-102 (SEMDEXA) Expected to be the First Product Approved to Treat Sciatica

Semnur Pharmaceuticals™
Getting Back to Normal

- SP-102 is a preservative free, surfactant free and particulate free viscous gel formulation of dexamethasone for sciatica (lumbosacral radicular pain).
- Extended local effect provides durable pain relief and significant improvement in functioning from a single injection with rapid onset.
- Improvement against placebo over 4 weeks and continued effect over 12 weeks with reduced use of rescue therapy.
- Good safety profile for single and repeat injections.
- Common epidural delivery by minimally invasive procedure conducted in outpatient pain clinics.
- Stable at refrigerated temperature in a prefilled syringe.





SP-102 Differentiated Product Profile & Positioning

Semnur Pharmaceuticals™
Getting Back to Normal

Important Treatment Attributes	SP-102	Kenalog (triamcinolone)	Depo-Medrol (methylprednis-olone)	Dexameth-asone	Celestone (betamethasone)
FDA-approved for lumbosacral radicular pain	✓	–	–	–	–
Robust clinical data demonstrating safety and efficacy	✓	–	–	–	–
Fast onset of effect in LR with low spread	✓	–	–	–	–
Confirmed duration of efficacy	✓	–	–	–	–
Reduction in disability in LR	✓	–	–	–	–
Safe to administer repeat injections	✓				
Novel formulation with prolonged residency time at injection site	✓	–	–	–	–
No Surfactants	✓	–	–	–	–
No Preservatives	✓	–	–	–	–
No Particulates	✓	–	–	✓	–
Prefilled Syringe	✓	–	–	–	–

SP-102 (SEMDEXA) Coverage – Public Payers Overview

Semnur Pharmaceuticals™
Getting Back to Normal

LR ESI products are covered by public payers (Medicare, Medicaid, and Medicare Advantage) as a physician-administered drug.

Public Payer Coverage

	Pharmacy Benefits	Medical Benefits
Drug Administration	• Self-administered • Oral or injectable	• ***Physician-administered*** • Infusion or injectable
Coverage Guidance and Relevant Medicare part(s)	• Formulary (A list of prescription drugs covered) • Part D	• Medical policy (guidelines for what medical services, procedures, devices and drugs may be eligible for coverage) • Parts A, B, and C (i.e., Medicare Advantage)*
Site of Care Setting	• Patient's home (typically)	• Hospital inpatient, hospital outpatient, physician office, ambulatory surgery center (ASC), independent diagnostic testing facility, SPP
Distribution Method	• Retail pharmacy • Specialty pharmacy	• Wholesaler • Specialty distributor (SD) • Direct-to-provider (drop-ship)
Patient Cost-share	• Copay/coinsurance for office visit • Copay/coinsurance for the drug	• Some plans may require additional cost-sharing beyond the office visit

Physician-administered Drug Overview

- ***Physician-administered drug*** is an outpatient drug other than a vaccine that is typically administered by a health care provider in a physician's office or other outpatient clinical setting
- Providers can bill physician-administered drugs to the ***medical benefits*** of ***Medicare*** and the state ***Medicaid*** program with ***NDC and HCPCS code***, if it's medically necessary and meets the guidelines
- Physician-administered drug is billed by ***J codes;*** a ***miscellaneous J code*** may be applied to in short-term post launch (typically 6 months**) until the new J code is established
- Physician-administered drugs may be eligible for a ***rebate*** (typically ~24%**) as long as the drug meets the definition of a covered ***outpatient drug*** and is ***not billed as part of a bundle service***
- The state Medicaid's payment methodology must be approved by CMS and may vary among states

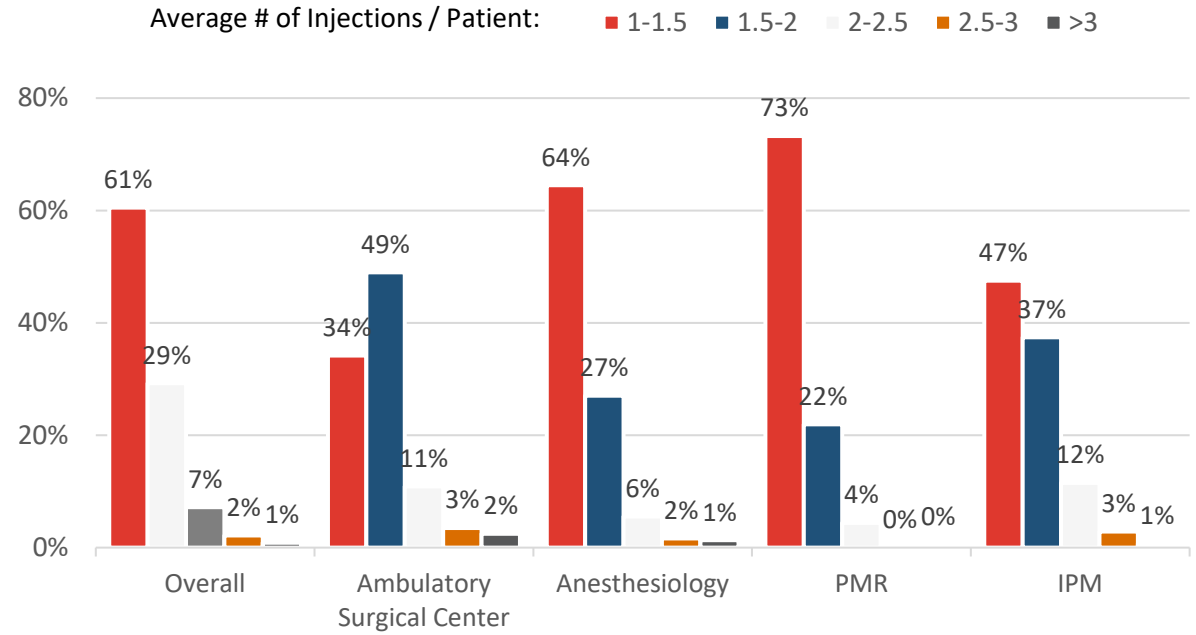
Source: 1. Syneos SME insights, 2. Medicaid and CHIP Payment and Access Commission: https://www.macpac.gov/physician-administered-drugs/
*Medicare Part C may also include a prescription drug benefit that may be managed under a pharmacy benefit; **Based on Syneos SME insights

SP-102 (SEMDEXA) Forecast
Patient Visit – ESI Volume Analysis

Semnur Pharmaceuticals™
Getting Back to Normal

The number of ESIs performed in ambulatory surgical centers (ASCs) is higher than that in other settings/physician specialties in 2018.

Average Injection Number by HCP Specialty (2018)[1]



Average	1.59	**1.77**	1.57	1.43	1.66
Median	1.40	**1.61**	1.35	1.35	1.51

Key Points

- On average, ***~60%*** of total physicians perform ***1.5 or fewer ESIs*** per patient in 2018
- ***Physicians from ASCs*** perform ***more*** ESIs per patient (i.e., average and median) vs. non-ASC physicians
  - ***>50% (i.e. 66%)*** of ASC physicians perform ***more than 1.5*** ESIs per patient
- ***Interventional Pain Medicine*** perform the ***highest*** number of ESIs (i.e., average and median) among all ***major physician specialties***

Ambulatory Surgical Centers and IPMs are potential targets for high-volume prescribers for SP-102.

Source: Medicare Provider Utilization and Payment Data: https://www.cms.gov/research-statistics-data-systems/medicare-provider-utilization-and-payment-data/medicare-provider-utilization-and-payment-data-physician-and-other-supplier/physician-and-other-supplier-data-cy-2018

Off-Label Steroids Bolded Warning Against Epidural Use

Semnur Pharmaceuticals™
Getting Back to Normal

	Drug	Formulation	Potential Issues
Currently Used	**Depomedrol**	• Methylprednisolone acetate • Contains polyethylene glycol + benzyl alcohol	***The safety and effectiveness of epidural administration of corticosteroids have not been established and corticosteroids are not approved for this use*** • Benzyl alcohol neurotoxicity
	Kenalog	• Triamcinolone acetonide • Contains benzyl alcohol	***The safety and effectiveness of epidural administration of corticosteroids have not been established and corticosteroids are not approved for this use*** • Neurotoxicity of benzyl alcohol
	Soluspan	• Betamethasone acetate 50% & Betamethasone sodium phosphate 50% • Contains benzalkonium chloride & EDTA	***The safety and effectiveness of epidural administration of corticosteroids have not been established and corticosteroids are not approved for this use*** • Neurotoxicity of benzalkonium chloride & EDTA
Less Used	**Decadron**	• Dexamethasone sodium phosphate • Benzyl alcohol	***The safety and effectiveness of epidural administration of corticosteroids have not been established and corticosteroids are not approved for this use*** • Benzyl alcohol neurotoxicity

- **All marketed injectable steroid products have bolded label warnings: "***serious neurologic events, some resulting in death, have been reported with epidural injection" and that the "safety and effectiveness of epidural administration of corticosteroids have not been established"*
- All current ESI products have preservatives and/or surfactants

SEMDEXA – Broad Potential for Life Cycle Management

Semnur Pharmaceuticals™
Getting Back to Normal

Physicians indicated there is potential opportunity for spontaneous use of SEMDEXA outside of lumbar radiculopathy which could represent an additional upside of ~50-200%* over LR

Additional Uses

- Carpel Tunnel
- Trigger Point Injections
- Injections for Knee, Shoulders, Wrists, Ankles, Joints
- Cervical Radiculopathy
- Knee Arthritis
- Hip and Knee Replacements
- Complex Regional Pain Syndromes (CRPS)
- Lumbar Spinal Stenosis
- Acute Spinal Injury
- Discogenic Pain

*Assumes similar degree of utilization for additional indications

History of Serious Spinal Adverse Events Associated with ESIs:
Resulting FDA Warning in All Injectable Corticosteroid Product Labels

Semnur Pharmaceuticals™
Getting Back to Normal

1997-2014	90 serious (including fatal) neurological events following ESIs reported to FAERS
2014	FDA required warning for all injectable corticosteroid product labels "…injection of corticosteroids into the epidural space of the spine may result in rare but serious adverse events, including loss of vision, stroke, paralysis, and death."
2015	FDA convened panel of experts (Multidisciplinary Working Group –MWG) for Safe Use Initiative (SUI) to review existing evidence regarding neurological complications and publish recommendations to prevent neurological complications after ESIs

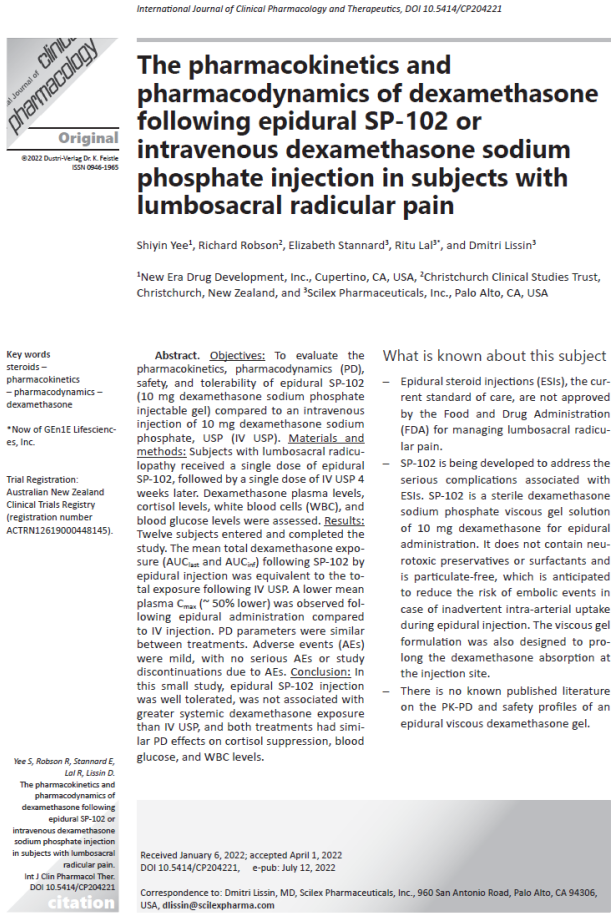
Serious neurologic AEs are associated with particulate steroids in particular; non-particulate steroids are recommended for ESI injections, but duration of pain relief is brief.

Reference: Cohen SP. Clin J Pain 2021;37:707–717
Reference: Nebojsa Nick Knezevic, MD, PhD Presentation on May 5, 2022 - Results from a Pivotal Phase 3, DB, R,Placebo-controlled, Multicenter Trial of SP-102, a Novel Dexamethasone Injectable Formulation, for the Treatment of Patients with Lumbosacral Radiculopathy (Sciatica)

SP-102 (SEMDEXA) Pharmacokinetic Bridging Trial

Semnur Pharmaceuticals™
Getting Back to Normal

- Epidural SP-102 injection was well tolerated
- Not associated with greater systemic dexamethasone exposure than IV dexamethasone at the same dose 10 mg (Reference Listed Drug)
  - Equivalent AUC
  - Lower mean plasma C_{max} (~ 50% lower)
- Both treatments had similar PD effects on cortisol suppression, blood glucose, and WBC levels.
- Trial supports 505(b)(2) NDA, bridging to known systemic safety of FDA approved IV dose.



International Journal of Clinical Pharmacology and Therapeutics, DOI 10.5414/CP204221

Original

©2022 Dustri-Verlag Dr. K. Feistle
ISSN 0946-1965

The pharmacokinetics and pharmacodynamics of dexamethasone following epidural SP-102 or intravenous dexamethasone sodium phosphate injection in subjects with lumbosacral radicular pain

Shiyin Yee[1], Richard Robson[2], Elizabeth Stannard[3], Ritu Lal[3*], and Dmitri Lissin[3]

[1]New Era Drug Development, Inc., Cupertino, CA, USA, [2]Christchurch Clinical Studies Trust, Christchurch, New Zealand, and [3]Scilex Pharmaceuticals, Inc., Palo Alto, CA, USA

Key words
steroids – pharmacokinetics – pharmacodynamics – dexamethasone

*Now of GEn1E Lifesciences, Inc.

Trial Registration: Australian New Zealand Clinical Trials Registry (registration number ACTRN12619000448145).

Abstract. Objectives: To evaluate the pharmacokinetics, pharmacodynamics (PD), safety, and tolerability of epidural SP-102 (10 mg dexamethasone sodium phosphate injectable gel) compared to an intravenous injection of 10 mg dexamethasone sodium phosphate, USP (IV USP). Materials and methods: Subjects with lumbosacral radiculopathy received a single dose of epidural SP-102, followed by a single dose of IV USP 4 weeks later. Dexamethasone plasma levels, cortisol levels, white blood cells (WBC), and blood glucose levels were assessed. Results: Twelve subjects entered and completed the study. The mean total dexamethasone exposure (AUC_{last} and AUC_{inf}) following SP-102 by epidural injection was equivalent to the total exposure following IV USP. A lower mean plasma C_{max} (~ 50% lower) was observed following epidural administration compared to IV injection. PD parameters were similar between treatments. Adverse events (AEs) were mild, with no serious AEs or study discontinuations due to AEs. Conclusion: In this small study, epidural SP-102 injection was well tolerated, was not associated with greater systemic dexamethasone exposure than IV USP, and both treatments had similar PD effects on cortisol suppression, blood glucose, and WBC levels.

What is known about this subject

- Epidural steroid injections (ESIs), the current standard of care, are not approved by the Food and Drug Administration (FDA) for managing lumbosacral radicular pain.
- SP-102 is being developed to address the serious complications associated with ESIs. SP-102 is a sterile dexamethasone sodium phosphate viscous gel solution of 10 mg dexamethasone for epidural administration. It does not contain neurotoxic preservatives or surfactants and is particulate-free, which is anticipated to reduce the risk of embolic events in case of inadvertent intra-arterial uptake during epidural injection. The viscous gel formulation was also designed to prolong the dexamethasone absorption at the injection site.
- There is no known published literature on the PK-PD and safety profiles of an epidural viscous dexamethasone gel.

Yee S, Robson R, Stannard E, Lal R, Lissin D. The pharmacokinetics and pharmacodynamics of dexamethasone following epidural SP-102 or intravenous dexamethasone sodium phosphate injection in subjects with lumbosacral radicular pain. Int J Clin Pharmacol Ther. DOI 10.5414/CP204221

citation

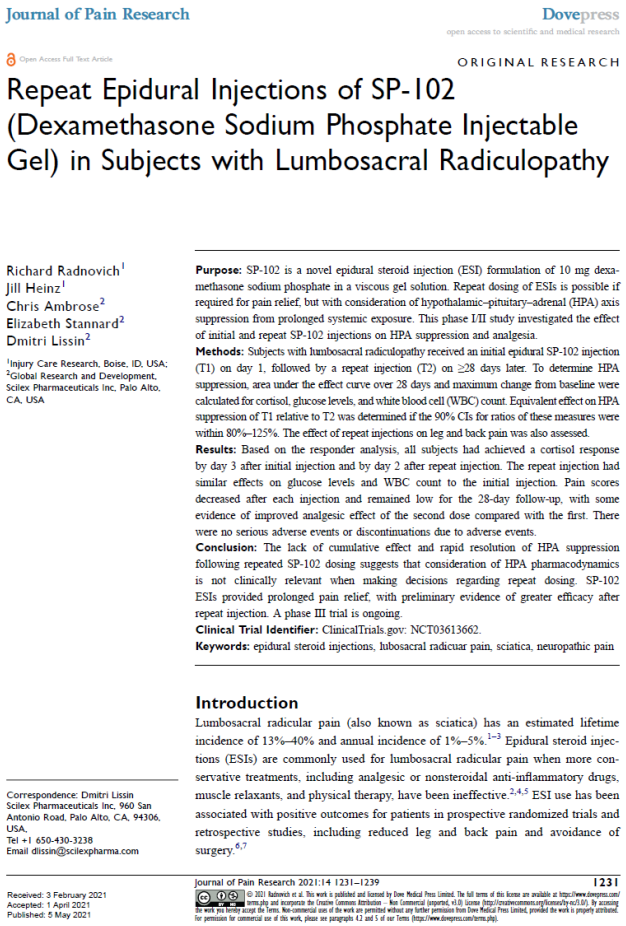
Received January 6, 2022; accepted April 1, 2022
DOI 10.5414/CP204221, e-pub: July 12, 2022

Correspondence to: Dmitri Lissin, MD, Scilex Pharmaceuticals, Inc., 960 San Antonio Road, Palo Alto, CA 94306, USA, dlissin@scilexpharma.com

SP-102 (SEMDEXA) Phase 2: Repeat Dose PD trial

Semnur Pharmaceuticals™
Getting Back to Normal

- The repeat injection had similar effects on cortisol suppression time (~5 days), glucose levels and WBC count. No cumulative effect.
- There were no SAEs or discontinuations due to adverse events.
- SP-102 provided prolonged pain relief, with preliminary evidence of greater efficacy after repeat injection.



Journal of Pain Research
Dovepress
open access to scientific and medical research
Open Access Full Text Article
ORIGINAL RESEARCH

Repeat Epidural Injections of SP-102 (Dexamethasone Sodium Phosphate Injectable Gel) in Subjects with Lumbosacral Radiculopathy

Richard Radnovich[1]
Jill Heinz[1]
Chris Ambrose[2]
Elizabeth Stannard[2]
Dmitri Lissin[2]

[1]Injury Care Research, Boise, ID, USA; [2]Global Research and Development, Scilex Pharmaceuticals Inc, Palo Alto, CA, USA

Purpose: SP-102 is a novel epidural steroid injection (ESI) formulation of 10 mg dexamethasone sodium phosphate in a viscous gel solution. Repeat dosing of ESIs is possible if required for pain relief, but with consideration of hypothalamic–pituitary–adrenal (HPA) axis suppression from prolonged systemic exposure. This phase I/II study investigated the effect of initial and repeat SP-102 injections on HPA suppression and analgesia.
Methods: Subjects with lumbosacral radiculopathy received an initial epidural SP-102 injection (T1) on day 1, followed by a repeat injection (T2) on ≥28 days later. To determine HPA suppression, area under the effect curve over 28 days and maximum change from baseline were calculated for cortisol, glucose levels, and white blood cell (WBC) count. Equivalent effect on HPA suppression of T1 relative to T2 was determined if the 90% CIs for ratios of these measures were within 80%–125%. The effect of repeat injections on leg and back pain was also assessed.
Results: Based on the responder analysis, all subjects had achieved a cortisol response by day 3 after initial injection and by day 2 after repeat injection. The repeat injection had similar effects on glucose levels and WBC count to the initial injection. Pain scores decreased after each injection and remained low for the 28-day follow-up, with some evidence of improved analgesic effect of the second dose compared with the first. There were no serious adverse events or discontinuations due to adverse events.
Conclusion: The lack of cumulative effect and rapid resolution of HPA suppression following repeated SP-102 dosing suggests that consideration of HPA pharmacodynamics is not clinically relevant when making decisions regarding repeat dosing. SP-102 ESIs provided prolonged pain relief, with preliminary evidence of greater efficacy after repeat injection. A phase III trial is ongoing.
Clinical Trial Identifier: ClinicalTrials.gov: NCT03613662.
Keywords: epidural steroid injections, lubosacral radicuar pain, sciatica, neuropathic pain

Introduction

Lumbosacral radicular pain (also known as sciatica) has an estimated lifetime incidence of 13%–40% and annual incidence of 1%–5%.[1–3] Epidural steroid injections (ESIs) are commonly used for lumbosacral radicular pain when more conservative treatments, including analgesic or nonsteroidal anti-inflammatory drugs, muscle relaxants, and physical therapy, have been ineffective.[2,4,5] ESI use has been associated with positive outcomes for patients in prospective randomized trials and retrospective studies, including reduced leg and back pain and avoidance of surgery.[6,7]

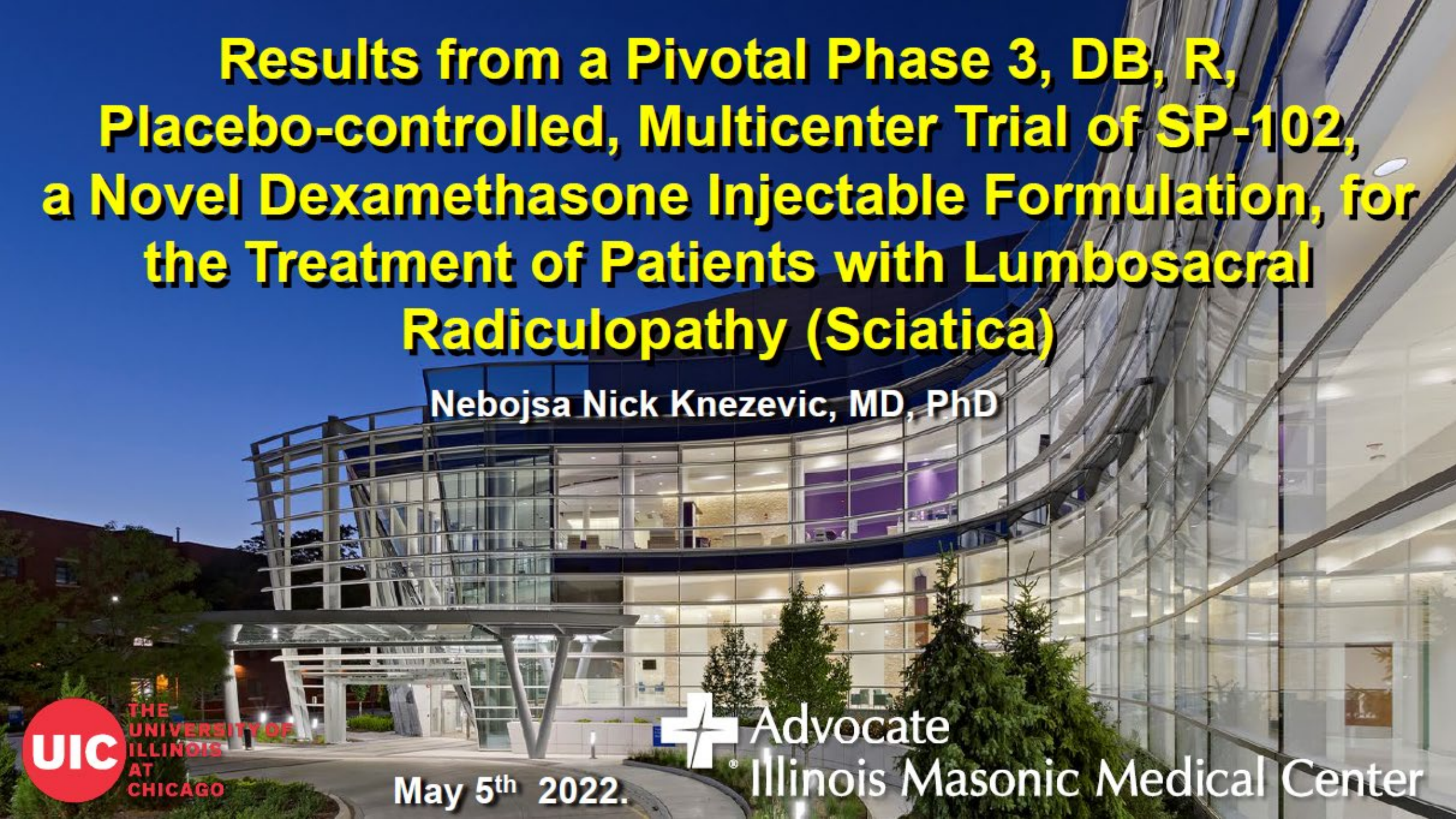
Correspondence: Dmitri Lissin
Scilex Pharmaceuticals Inc, 960 San Antonio Road, Palo Alto, CA, 94306, USA,
Tel +1 650-430-3238
Email dlissin@scilexpharma.com

Received: 3 February 2021
Accepted: 1 April 2021
Published: 5 May 2021

© 2021 Radnovich et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v3.0) License (http://creativecommons.org/licenses/by-nc/3.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

Results from a Pivotal Phase 3, DB, R, Placebo-controlled, Multicenter Trial of SP-102, a Novel Dexamethasone Injectable Formulation, for the Treatment of Patients with Lumbosacral Radiculopathy (Sciatica)

Nebojsa Nick Knezevic, MD, PhD



May 5th 2022.

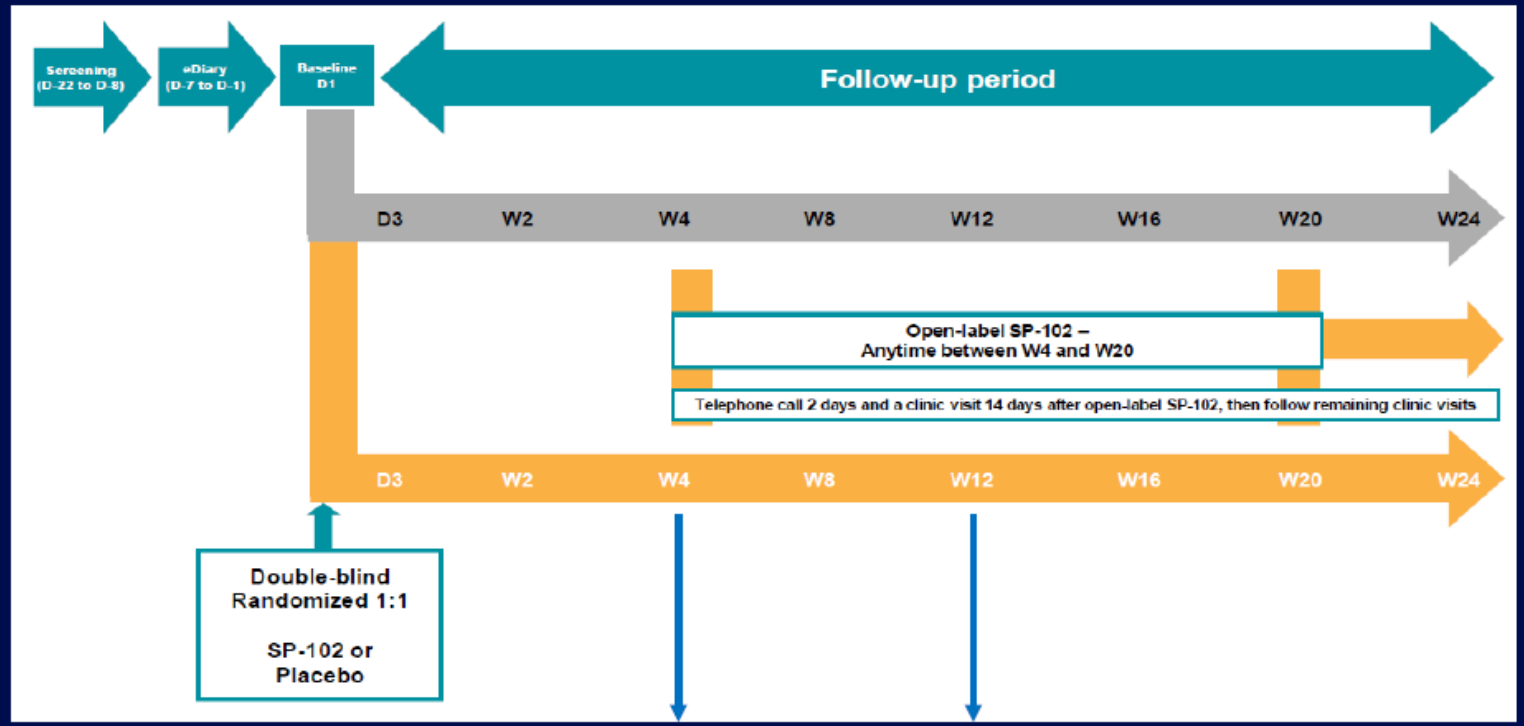
SP-102 (SEMDEXA) C.L.E.A.R. Trial Schema

Semnur Pharmaceuticals™
Getting Back to Normal

C.L.E.A.R. Trial Design

Inclusion

- ✓ Radicular leg pain episode (4-9 NPRS) **6 weeks-9 months**
- ✓ MRI confirmed within 9 months
- ✓ No prior ESI
- ✓ No opioids or NSAIDs
- ✓ Stable, >4 avg NPRS pain in 21d screening



Primary Endpoint
Change in mean leg pain (NPRS) over first 4 weeks

Secondaries (W2, W4, W8, W12) Leg pain (NPRS, avg & worst pain), disability (ODI), time to repeat injection

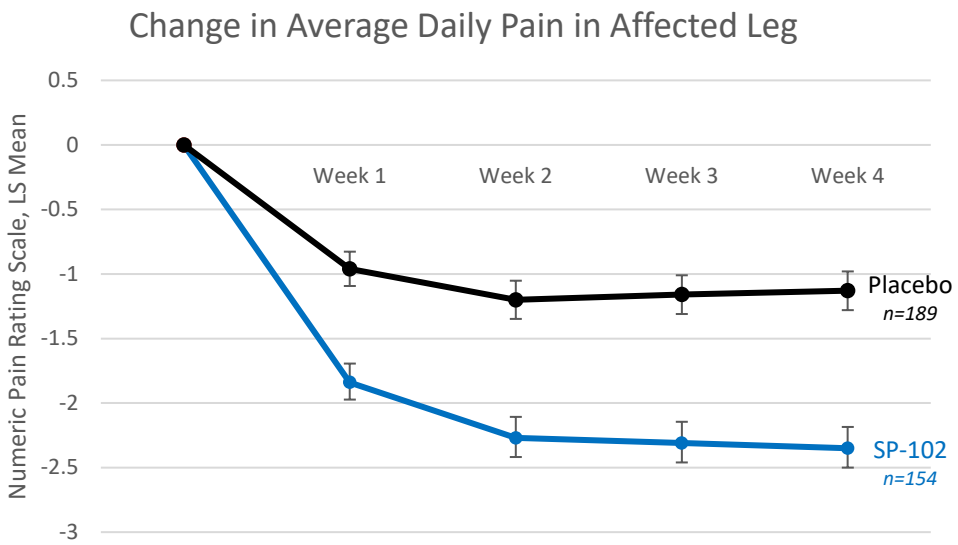
SP-102 (SEMDEXA) C.L.E.A.R. Trial Met Primary Endpoint

(Corticosteroid Lumbar Epidural Analgesia in Radiculopathy)

Semnur Pharmaceuticals™
Getting Back to Normal

- Largest prospective, double-blind, randomized study in Sciatica (n=401)
- The trial met primary, key secondary and other secondary endpoints with statistical significance over placebo in ITT and mITT populations
  - Meaningful Standardized Effect Size (ITT 0.28, mITT 0.68)
  - Improvement in efficacy responses observed for mITT population when patients receive a fluoroscopically verifiable injection (needle placement and contrast flow), consistent with clinical practice.
- Achieved all study objectives, up to 3 months duration of effect with a single injection
- Demonstrated safety profile of SP-102

Primary Endpoint (mITT)



Comparison: SP-102 vs. Placebo	
Over 4 Weeks, LS Mean (SE)	-1.08 (0.17)
95% CI	-1.42, -0.75
p-value	<0.001***

The analysis used a restricted maximum likelihood (REML) based mixed model for repeated measures (MMRM) with fixed effects for treatment (SP-102 or placebo), week, site, Pain Catastrophizing Scale group (<30 or ≥30), baseline averaged daily leg pain score, and treatment-by-week interaction.

SP-102 (SEMDEXA) C.L.E.A.R. Trial Secondary Endpoints (ITT)

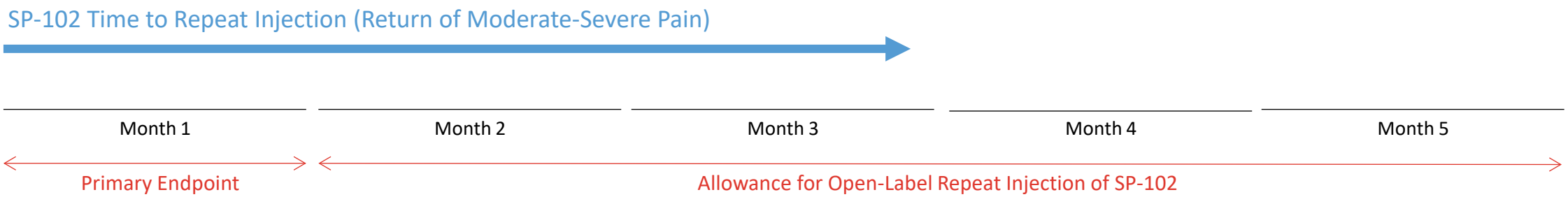
Semnur Pharmaceuticals™
Getting Back to Normal

- Key Secondary Endpoint
  - The Oswestry Disability Index (ODI) - gold standard for measuring degree of disability and estimating quality of life, contains 10 topics concerning intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel.
  - Mean change in ODI from baseline, the LS mean treatment difference (SE) for SP-102 was -3.38 (1.388) units [95% CI: -6.11, -0.65] compared to placebo (P=0.015).
  - ODI -8.88 point reduction from baseline exceeds the established[1] minimal clinically important difference of -8.
- Other secondary endpoints
  - Worst pain in affected leg at Week 4 (P=0.004) and over 4 weeks (P=0.001),
  - Average pain in lower back (P=0.035),
  - BPI-SF for pain severity (P=0.003) and pain interference (P=0.049),
  - PGIC (P<0.001) and CGIC (P<0.001),
  - Proportion of patients achieving 30% response (P=0.002)

[1]Maughan EF, Lewis JS. Outcome measures in chronic low back pain. Eur Spine J 2010;19(9):1484-94.

SP-102 (SEMDEXA) C.L.E.A.R. Trial – Effect Duration and Safety

Semnur Pharmaceuticals™
Getting Back to Normal



- SP-102 showed continued reduction of pain beyond one month, and the median time to open-label repeat injection was 99 days (ITT, 95% CI: 71, 100 days) according to a Kaplan-Meier estimation.
- By contrast, off-label injectable steroids typically provide pain relief for periods ranging from less than a week and up to one month, and then a repeat injection may be required.

SP-102 (SEMDEXA) C.L.E.A.R. Safety Summary

Semnur Pharmaceuticals™
Getting Back to Normal

- No AEs of special interest (paraplegia, hematoma, infection)
- No SAEs related to drug or injection procedure
- No meaningful differences in physical examinations, vital signs, or laboratory parameters between treatment groups

TEAEs Prior to Second Injection	SP-102 (N=202) Subjects n (%)	SP-102 (N=202) Events n	Placebo (N=199) Subjects n (%)	Placebo (N=199) Events n
Any TEAE	60 (29.7)	104	42 (21.1)	68
TEAE with >2% Incidence				
Headache	13 (6.4)	17	11 (5.5)	11
Injection site pain	4 (2.0)	4	0	0
Upper respiratory tract infection	2 (1.0)	2	4 (2.0)	4
Hypertension	4 (2.0)	4	1 (0.5)	2

SP-102 Key Milestones

Semnur Pharmaceuticals™
Getting Back to Normal

1. Toxicology program complete
2. Pharmacokinetic bridge established to Reference Listed Drug
3. Phase II, additional PK / PD / Safety of repeat injection trial completed
4. Phase III CLEAR Trial completed
5. NDA 505(b)(2) application confirmed
6. Additional Phase III design confirmed with FDA

Research Paper

PAIN 00 (2024) 1–12

PAIN®

OPEN

A randomized, placebo-controlled trial of long-acting dexamethasone viscous gel delivered by transforaminal injection for lumbosacral radicular pain

Alan Miller[a], Kenneth D. Candido[b], Nebojsa Nick Knezevic[b], José Rivera[c], Paul Lunseth[d], Dennis J. Levinson[e], Ferdinand Formoso[f], Daneshvari Solanki[g], Edward Tavel[h], Angela Krull[i], Richard Radnovich[j], Daniel Burkhead[k], Dmitri Souza[l], Standiford Helm[m], Nathaniel Katz[n], Robert H. Dworkin[o], Steven P. Cohen[p], James P. Rathmell[q], Asokumar Buvanendran[r], Joshua Levin[s], Elizabeth Stannard[t], Chris Ambrose[u], Mark Jaros[v], Kip Vought[t], Dmitri Lissin[u,*]

Abstract

Epidural steroid injections are used to treat lumbosacral radicular pain. However, there are no Food and Drug Administration–approved corticosteroids for lumbosacral radicular pain and all currently available injectable corticosteroids carry safety warnings about their use in epidural steroid injection procedures. SP-102 (dexamethasone injectable viscous gel) was developed to provide a safer option with extended local effect. In a randomized, double-blind, placebo-controlled, multicenter trial, 401 patients with moderate-to-severe leg pain from unilateral intervertebral lumbar disc herniation were randomized (1:1) to receive transforaminal SP-102 or sham intramuscular (IM) placebo injection and followed for 24 weeks. If clinically warranted, a repeat open-label SP-102 injection was allowed between 4 and 20 weeks for both groups. Primary and key secondary end points were change in average daily pain on the Numeric Pain Rating Scale in the affected leg and disability measured by Oswestry Disability Index over 4 weeks. Other secondary end points included time to repeat injection, pain, and quality of life assessments. Over 4 weeks, SP-102 demonstrated statistically significant pain relief compared with placebo (least-squares mean group difference −0.52 [SE 0.163] [$P = 0.002$]) in the intent-to-treat population. Oswestry Disability Index mean improvement was −3.38 (1.388) (least-squares mean group difference [SE]) for SP-102 vs placebo ($P = 0.015$). Median time to repeat injection was 84 days for SP-102 vs 58 days for placebo ($P = 0.001$). Most other secondary end points were statistically significant for SP-102 compared with placebo. There were no serious adverse events related to study medication or procedure, no adverse events leading to death, and no AEs of special interest (paraplegia, hematoma, or infection).

Trial Registration

ClinicalTrials.gov Identifier: NCT03372161.

Keywords: Epidural Steroid Injections, ESI, Epidural, Anesthesia, Dexamethasone, sciatica, Lumbar radiculopathy, SP-102, Dexamethasone injectable viscous gel, Lumbosacral radiculopathy, LSR

Downloaded from http://journals.lww.com/pain by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 06/14/2024

Semnur Pharmaceuticals™
Getting Back to Normal

Summary Investment Highlights

Semnur Pharmaceuticals™
Getting Back to Normal

- ✓ Huge Unmet Needs Without Approved Products to Treat for Sciatica
- ✓ Worldwide Commercial Rights to SP-102
- ✓ Strong Proprietary Platform with Issued IP and High Barriers to Entry
- ✓ Established Reimbursement Access
- ✓ Blockbuster Potential With Limited Capital Required for Commercialization