# Long-term improvements in serum uric acid levels, gout symptoms, and safety up to 12-months with SEL-212 in gout refractory to conventional therapy: Results from the DISSOLVE I Phase 3, double-blind, placebo-controlled clinical trial

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## CONCLUSIONS

- High-dose (HD) and low-dose (LD) SEL-212 provided substantial and consistent reductions in serum uric acid (sUA) from baseline to treatment period (TP) 12 in responders.
- Most of the patients responding to SEL-212 at TP 6 maintained a response at TPs 9 and 12.
- Numerical improvements from baseline to TP 6 in swollen/tender joint counts, the proportion of patients without gout flare, and physical functioning were maintained at TP 12.
- Both SEL-212 doses were well tolerated with no new safety signals in the extension phase.
- Investigational SEL-212 has the potential to be an effective once-monthly therapy for use up to 12 months in patients with refractory gout.

## INTRODUCTION

- Uricase-based therapies may profoundly lower sUA levels in people with gout refractory to conventional treatments; use is limited by immunogenicity-related efficacy reductions and infusion reactions.[1]
- SEL-212 is an investigational, once-monthly uricase-based therapy comprising sequential infusions of tolerogenic nanoparticles containing sirolimus (SEL-110) followed by a novel pegylated uricase (pegadricase; SEL-037).[2-4]
- Co-administration of SEL-110 with SEL-037 mitigates uricase immunogenicity in clinical studies, thereby enabling sustained sUA control without the need for broader immunosuppression.[2-4]
- Six-month results from the DISSOLVE I trial found that once-monthly infusions of SEL-212 (HD and LD) were well tolerated and met the primary endpoint of achieving sUA <6 mg/dL for ≥80% of the time (response rate) during TP 6 in adults with gout refractory to conventional treatments.[5]
- Response rates at TP 6 were significantly higher for HD and LD SEL-212 (56% and 48%) vs. placebo (4%) (p<0.0001 for both doses vs. placebo).
- This poster describes the safety and efficacy of SEL-212 up to 12 months in DISSOLVE I.

## METHODS

### Participants

- US adults with sUA ≥7 mg/dL and inadequate disease control despite medically appropriate doses of conventional gout therapies.[5]
- History of symptomatic gout defined as:
  - ≥3 gout flares within 18 months prior to screening, **OR**
  - ≥1 tophus, **OR**
  - Current diagnosis of gouty arthritis.
- For response rates at each timepoint, intercurrent events leading to trial drug discontinuations and those related to the use of prohibited medication that lower sUA levels were considered as treatment failures using the composite strategy. Treatment policy was used to analyse other intercurrent events.
- Missing responder status was multiple imputed using a predictive mean matching approach.
- Descriptive statistics were used to summarise all other endpoints.

### DISSOLVE I trial design (NCT04513366)

- Randomised, double-blind, placebo-controlled, parallel-arm phase 3 trial in the USA.
- Patients received sequential infusions of HD SEL-212 (0.15 mg/kg SEL-110 and 0.2 mg/kg SEL-037), LD SEL-212 (0.1 mg/kg SEL-110 and 0.2 mg/kg SEL-037) or placebo every 28 days for 6 months (TP 1-6).
- Patients completing TP 6 were eligible to enter the 6-month blinded extension phase (TP 7-12) on the same treatment for up to an additional 6 months.
  - Patients who met the stopping rule during the main study period or during the extension phase discontinued study drug but continued study visits and were included in the analyses.
- All patients received infusion reaction and gout flare prophylaxis.
- Trial treatment was discontinued if the following **stopping rule** was met: sUA <2.0 mg/dL 1-h after infusion of the second component of study drug during TP 1 **AND** >1.0 mg/dL at Day 21 of TP 1 **OR** >6.0 mg/dL at Day 21 of TP 2-11.

### Extension study outcomes

- **12-month** response rates, sUA levels in responders and non-responders, swollen/tender joint counts, proportion of patients without gout flares, and safety (treatment-emergent adverse events [TEAE] and adverse events of special interest [AESI]).

## RESULTS

### Patient disposition

- 115 patients were randomised and 112 dosed; 38 received HD, 37 LD, and 37 placebo (Intent-to-treat [ITT] set);
  - 80 (27 [HD], 27 [LD], 26 [placebo]) patients completed TP 6 and entered the extension phase (extension evaluable [EE] set).
  - 64 (23 [HD], 19 [LD], 22 [placebo]) patients completed TP 12.
- The stopping rule was met by 8 (21.1%) (HD), 15 (40.5%) (LD), and 1 (2.7%) (placebo) patient during TP 1-6 (ITT set) compared to 1 (3.7%), 1 (3.7%), and 0 patients during TP 7-12 (EE set).

### Baseline demographics and disease characteristics

- Baseline demographics and characteristics were similar for the ITT set (**Table 1**) and the EE set.
- Most patients were male, white, aged ≥50 years, and >50% had tophi at baseline.

**Table 1. Patient characteristics and demographics at baseline (ITT set)**

| | High-dose SEL-212 (N=38) | Low-dose SEL-212 (N=37) | Placebo (N=37) |
|---|---|---|---|
| Age, years, median (range) | 54 (28–77) | 55 (35–79) | 52 (36–75) |
| BMI, kg/m$^2$, mean (SD) | 34.7 (6.4) | 33.9 (7.5) | 33.4 (6.3) |
| Gender, male, n (%) | 35 (92.1) | 35 (94.6) | 37 (100.0) |
| Race, n (%) | | | |
| White | 27 (71.1) | 28 (75.7) | 22 (59.5) |
| Black/African American | 9 (23.7) | 6 (16.2) | 7 (18.9) |
| Asian | 0 | 1 (2.7) | 3 (8.1) |
| Other | 2 (5.3) | 2 (5.4) | 5 (13.5) |
| Time since gout diagnosis, years, mean (SD) | 14.3 (10.5) | 11.9 (10.0) | 12.4 (9.6) |
| Patients with tophi at baseline, n (%) | 22 (57.9) | 21 (56.8) | 21 (56.8) |
| sUA level, mg/dL, mean (SD)[a] | 8.7 (1.4) | 8.4 (1.3) | 8.3 (1.5) |
| Prior ULT, n (%) | 30 (78.9) | 26 (70.3) | 25 (67.6) |
| Tender joint count, mean (SD) | n=36<br>1.9 (5.1) | n=33<br>3.5 (6.4) | n=33<br>2.6 (9.9) |
| Swollen joint count, mean (SD) | n=35<br>2.0 (4.3) | n=33<br>3.6 (7.5) | n=33<br>1.0 (3.4) |
| eGFR, mL/min/1.73m$^2$, mean (SD) | 71.3 (18.1) | 77.8 (19.4) | 74.4 (19.2) |
| SF-36 physical component summary score, mean (SD) | 39.7 (10.9) | 39.9 (9.9) | 37.7 (9.2) |
| Total HAQ-DI score, mean (SD) | 0.79 (0.67) | 0.78 (0.54) | 0.73 (0.58) |
| HAQ-DI pain score, mean (SD) | 31.2 (28.84) | 32.3 (28.11) | 32.7 (28.88) |

[a]sUA levels as assessed at screening. BMI, body mass index; eGFR, estimated glomerular filtration rate; HAQ-DI, Health assessment questionnaire-disability index; ITT, intent-to-treat; n, number; SD, standard deviation; SF-36, Short form health survey; sUA, serum uric acid; ULT, urate-lowering therapy. HAQ-DI is scored from 0 (no disability) to 3 (severe disability). HAQ-DI pain score is scored from 0 (no pain) to 100 (maximum pain). SF-36 is scored from 0 to 100 (higher scores indicate better health state).

### Treatment response

- **Response rates** were significantly higher for SEL-212 vs. placebo at all timepoints (**Figure 1**).
- 14/18 (77.8%) (HD) and 14/16 (87.5%) (LD) responders at TP 6 continued to respond to treatment at TP 9 and 12/18 (66.7%) (HD) and 12/16 (75.0%) (LD) responders at TP 6 maintained a response at TP 12.

### sUA control

- For responders, **mean sUA** was reduced from ≥8.5 mg/dL at baseline to ≤0.2 mg/dL within 4.5 h of SEL-212 infusion and was maintained <2 mg/dL from TP 1 to TP 12.
- **sUA levels** remained >6 mg/dL for all but 2 of the patients in the placebo arm; 1 achieved sUA control during TP 6 and the other during TP 12.

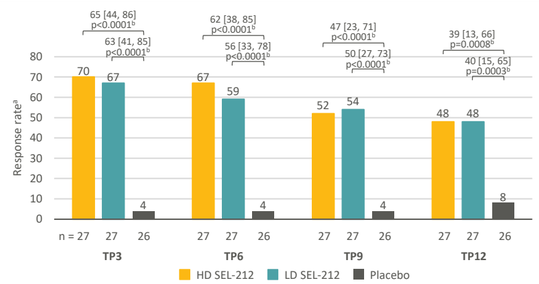
### Swollen/tender joints

- Mean ± SD **swollen joint counts** were reduced from 2.0 ± 4.43 (HD), 3.6 ± 7.51 (LD), and 1.0 ± 3.37 (placebo) at baseline to 1.1 ± 4.20 (HD), 0.3 ± 1.26 (LD), and 0.2 ± 0.88 (placebo) at TP 6, with further reductions at TP 12 (0.9 ± 3.83 [HD], 0.1 ± 0.33 [LD], and 0 ± 0.21 [placebo]).
- Mean ± SD **tender joint counts** were reduced from 1.9 ± 5.09 (HD), 3.5 ± 6.41 (LD), and 2.6 ± 9.92 (placebo) at baseline to 0.6 ± 2.19 (HD), 0 ± 0.21 (LD), and 0.2 ± 0.47 (placebo) at TP 6. Reductions at TP 6 were maintained at TP 12 (0.8 ± 3.33 [HD], 0.1 ± 0.33 [LD], and 0.2 ± 0.50 [placebo]).

### Gout flares

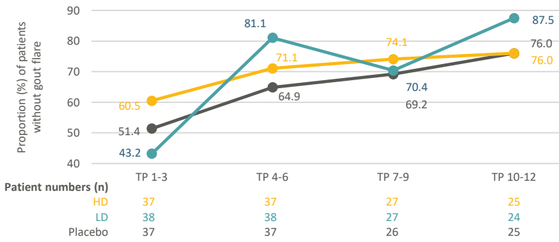
- The proportions of patients without gout flares on treatment increased over time (**Figure 2**).

**Figure 1. Response rates over time (EE Set)**




CI, confidence interval; EE, extension evaluable; HD, high dose; LD, low dose; sUA, serum uric acid; TP, treatment period. [a]Responders were defined as subjects with sUA levels <6mg/dL for at least 80% of the time during the TP of interest. Subjects who withdrew from the study due to the stopping rule, AE, and COVID were considered non-responders. Percentages shown are averaged over multiple imputed datasets for missing sUA for withdrawal of consent, lost to follow-up, and other as per FDA guidance. [b]Difference vs placebo [97.5% CI] and p-value versus placebo group for each treatment group are indicated above each bracket.

**Figure 2. Proportion of patients without gout flares from TP 1-3 and TP 4-6 (ITT Set) and from TP 7-9 and TP 10-12 (EE Set)**

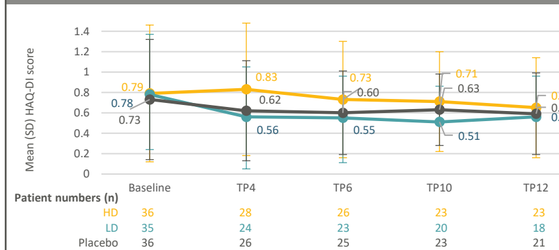



EE, extension-evaluable; HD, high-dose SEL-212; ITT, intent-to-treat; LD, low-dose SEL-212; TP, treatment period.

### Physical function

- Mean ± SD **HAQ-DI total scores** decreased from TP 1 to TP 6 and were maintained through TP 12 (**Figure 3**).

**Figure 3. Mean ± SD HAQ-DI scores from TP 1-12 (ITT Set)**




HAQ-DI, Health assessment questionnaire-disability index; HD, high-dose SEL-212; ITT, intent-to-treat; LD, low-dose SEL-212; n, number; SD, standard deviation; TP, treatment period. HAQ-DI is scored from 0 (no disability) to 3 (severe disability).

- Mean ± SD **HAQ-DI pain scores** decreased from 31.2 ± 28.8 (HD; n=28), 32.3 ± 28.1 (LD; n=30), and 32.7 ± 28.9 (placebo; n=32) at baseline to 16.7 ± 21.9 (n=19), 9.0 ± 14.2 (n=21), and 13.3 ± 18.2 (n=23), respectively, at TP6. Scores remained stable from TP 6 through TP 12 (17.3 ± 21.4 [n=16], 11.0 ± 21.5 [n=16], 20.1 ± 22.1 [n=20]).

## SAFETY

- Both SEL-212 doses were well tolerated with no new safety signals in the extension phase.
  - Treatment-related TEAEs affected 34.2% (HD), 40.5% (LD), and 32.4% (placebo) of patients during TP 1-6 vs. 11.1%, 22.2%, and 11.5%, respectively, during TP 7-12.
  - 4 serious treatment-related TEAEs occurred during TP 1-6 (2 gout flares [1 with HD; 1 with LD] and 2 anaphylaxis [both with LD]) and none during TP 7-12.
  - 1 death (motor-vehicle accident) deemed unrelated to study treatment occurred during the extension phase.
- Treatment-emergent AESI affecting >5% of SEL-212-treated patients included gout flares, hypertriglyceridemia, COVID-19 infections, stomatitis (including mouth ulceration and aphthous ulcer), and infusion-related reactions including anaphylaxis (**Table 2**).
  - All cases of stomatitis were mild/moderate and none resulted in patient withdrawal.

**Table 2. Summary of treatment-emergent AESI affecting >5% of patients in a single treatment arm (Safety set)**

| Treatment-emergent AESI[a] affecting >5% of patients in any treatment arm, n (%) | Main study (TP 1-6) | | | Extension phase (TP 7-12) | | |
|---|---|---|---|---|---|---|
| | High dose (N=38) | Low dose (N=37) | Placebo (N=37) | High dose (N=27) | Low dose (N=27) | Placebo (N=26) |
| Gout flare | **21 (50.0)** | **21 (56.8)** | **21 (56.8)** | **10 (37.0)** | **10 (37.0)** | **10 (38.5)** |
| Hypertriglyceridemia | **3 (7.9)** | 1 (2.7) | 1 (2.7) | **2 (7.4)** | **2 (7.4)** | 0 |
| IRR | | | | | | |
| IRR (24 h)[b] | **4 (10.5)** | **5 (13.5)** | **2 (5.4)** | 0 | **2 (7.4)** | 0 |
| IRR (within 1 h) | 1 (2.6) | **2 (5.4)** | 0 | NR | NR | NR |
| Anaphylactic reaction[c] | 0 | **2 (5.4)** | 0 | NR | NR | NR |
| Infections/infestations | **11 (28.9)** | **8 (21.6)** | **4 (10.8)** | **5 (18.5)** | **8 (29.6)** | **3 (11.5)** |
| COVID-19 | **2 (5.3)** | **3 (8.1)** | 1 (2.7) | **3 (11.1)** | **4 (14.8)** | 1 (3.8) |
| Upper RTI | **2 (5.3)** | **2 (5.4)** | 1 (2.7) | NR | NR | NR |
| Cellulitis | 1 (2.6) | 1 (2.7) | **2 (5.4)** | 0 | 1 (3.7) | 1 (3.8) |
| Folliculitis | **2 (5.3)** | 0 | 0 | 0 | 1 (3.7) | 0 |
| Streptococcal pharyngitis | **2 (5.3)** | 0 | 0 | NR | NR | NR |
| Stomatitis[d] | **5 (13.2)** | **3 (8.1)** | 0 | 0 | 1 (3.7) | 0 |
| Leukopenia | 0 | **2 (5.4)** | 0 | NR | NR | NR |

[a]AESIs include gout flares, infections, malignancies, viral infections, interstitial lung disease, stomatitis, IRRs including anaphylaxis, thrombosis (e.g., deep venous thrombosis, pulmonary embolism), and the following laboratory tests, if deemed clinically significant by the Project Investigator: hyperlipidemia, worsening of renal function tests, proteinuria, and leukopenia. AESI affecting ≥5% of patients are shown in bold. [b]IRRs over 24 h include reactions (including anaphylactic reactions) that occurred within 1 h and are defined as a trial drug-related adverse event that occurred within 24 h of completing study drug infusion. Allergic reaction/hypersensitivity were defined according to Rheumatology Common Toxicity Criteria, V 2.0. [c]IRRs suspected of being anaphylaxis were assessed according to the clinical criteria for the diagnosis of anaphylaxis based on the 2006 National Institute of Allergy and Infectious Diseases (NIAID)/Food Allergy and Anaphylaxis Network (FAAN) Symposium Criteria. [d]Also includes mouth ulceration and aphthous ulcer. AESI, adverse event of special interest; IRR, infusion-related reaction; RTI, respiratory tract infection; TP, treatment period; n, number of patients; NR, not reported.

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