# Nanoencapsulated Sirolimus plus Pegadricase (NASP) Demonstrates Long Term Efficacy and Safety in Patients with Uncontrolled Gout: Results from the 24-week Double-blind Extension of the Phase 3 DISSOLVE I Study

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## CONCLUSIONS

In DISSOLVE I, key findings among patients who completed six doses of NASP or placebo over 24 weeks and entered the blinded extension phase (defined as the '6D EE set') included:

- Patients receiving NASP experienced rapid sUA reductions 1 hour after the first infusion; in patients who remained on treatment, these reductions were sustained throughout the extension phase
- NASP-treated patients showed declining flare rates over time and lower cumulative flare frequency versus placebo
- NASP was generally well tolerated, with a high completion rate; in the extension phase, 71.4% of patients received all scheduled doses through Week 48

These results suggest a trend toward remission of uncontrolled gout symptoms with extended NASP treatment

## INTRODUCTION

- Uncontrolled gout is a systemic and progressive disease characterized by sustained elevation of sUA levels (>6 mg/dL) despite treatment with oral urate-lowering therapies (ULTs), leading to inflammation, painful flares, tophi and bone erosion,[1] making it more difficult to achieve remission[2]
- The Gout Hyperuricemia and Crystal-Associated Disease Network (G-CAN) recently proposed simplified gout remission criteria: sUA <6 mg/dL over 12 months, no gout flares over 12 months, and absence of subcutaneous tophi[2]
- NASP is a novel, investigational, every 4-week, sequential infusion therapy designed to reduce sUA levels in patients with uncontrolled gout. NASP consists of targeted immunomodulating, nanoencapsulated sirolimus (NAS; formerly SEL-110) co-administered with pegadricase (a pegylated uricase, formerly SEL-037)
- In pooled data from the Phase 3 DISSOLVE I and DISSOLVE II studies, NASP significantly reduced sUA and improved tophi compared to placebo, and decreased gout flares over time up to 6 months of treatment[3–5]

## OBJECTIVE

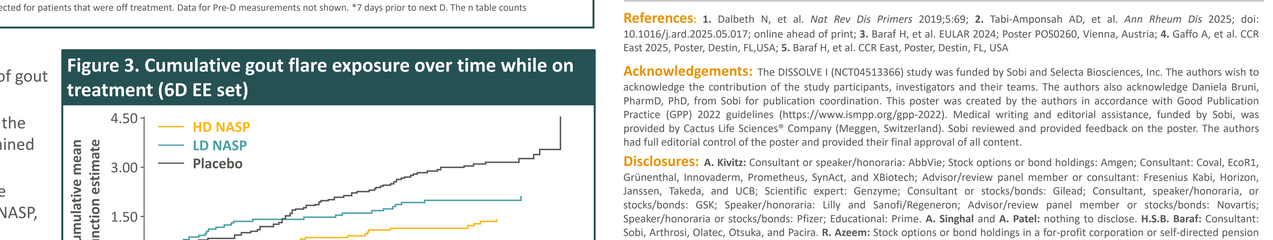
- This *post-hoc* analysis assessed the long-term efficacy and safety of NASP, through 48 weeks in patients in the DISSOLVE I study who received 6 doses of NASP or placebo during the 24-week main study period and continued into the blinded extension phase (defined as the '6D EE set')



## METHODS

- DISSOLVE I (NCT04513366) trial randomized patients 1:1:1 to one of two doses of NASP (high-dose [HD] or low-dose [LD]) or placebo. After each study drug administration, 4 weeks of observation followed for a total of 24 weeks during the main study. During this time, up to 6 doses of study drug could be administered
- Patients could enter a 24-week double-blind extension after the main study period (**Figure 1**)
- Patients meeting the stopping rule or discontinuing treatment who continued visits could restart ULT at Investigator discretion 60 days after the last dose

**Figure 1. DISSOLVE I (NCT04513366) study design**




## RESULTS

### Patient demographics and baseline characteristics

- Among patients in DISSOLVE I, 19 on HD NASP, 16 on LD NASP and 25 on placebo received all 6 doses of treatment during the main study period, and all entered the extension phase (**Table 1**)

**Table 1. Baseline characteristics (6D EE set, N=60)**

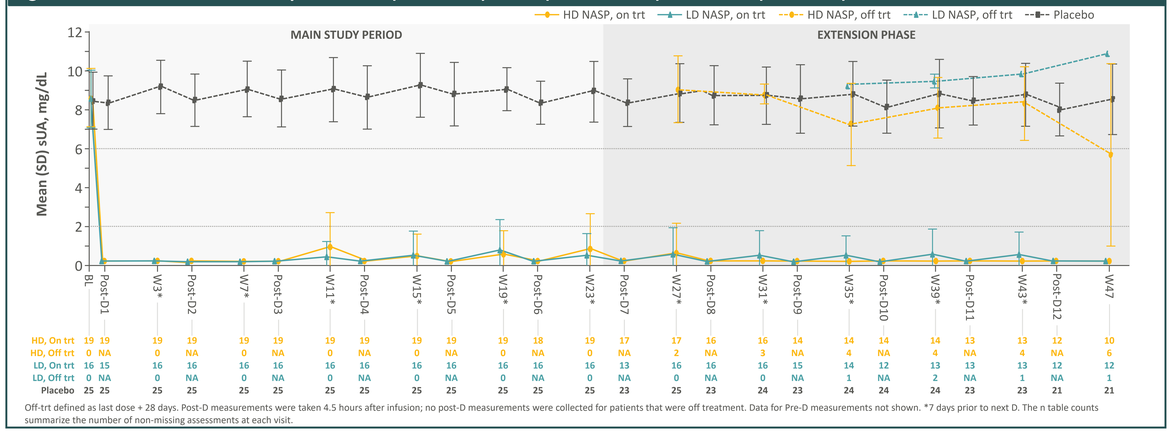
| | HD NASP (N=19) | LD NASP (N=16) | Placebo (N=25) |
|---|---|---|---|
| **Patient characteristics** | | | |
| Age, years, mean (SD) | 60.1 (10.39) | 54.3 (9.64) | 55.3 (11.33) |
| BMI, kg/m$^2$, mean (SD) | 34.2 (5.3) | 33.4 (6.7) | 34.4 (6.7) |
| Gender, male, n (%) | 16 (84.2) | 14 (87.5) | 25 (100) |
| Race, n (%) | | | |
| White | 14 (73.7) | 12 (75.0) | 16 (64.0) |
| Black or African American | 5 (26.3) | 4 (25.0) | 3 (12.0) |
| Other* | 0 | 0 | 6 (24.0) |
| **Disease characteristics** | | | |
| Years since gout diagnosis, mean (SD) | 14.6 (12.1) | 9.2 (8.3) | 13.6 (9.6) |
| sUA at baseline, mg/dL, mean (SD) | 8.41 (1.5) | 8.7 (1.1) | 8.3 (1.4) |
| Patients with tophi at baseline, n (%) | 7 (36.8) | 10 (62.5) | 15 (60.0) |
| eGFR, mL/min/1.73m$^2$, mean (SD) | 65.1 (17.9) | 73.0 (18.8) | 70.2 (17.8) |
| **Most common† comorbidities at baseline** | | | |
| Hypertension | 14 (73.7) | 8 (50.0) | 17 (68.0) |
| Hyperlipidemia | 8 (42.1) | 3 (18.8) | 9 (36.0) |
| Anxiety | 5 (26.3) | 1 (6.3) | 4 (16.0) |
| Diabetes‡ | 4 (21.1) | 0 | 3 (12.0) |
| Dyslipidemia | 4 (21.1) | 0 | 1 (4.0) |
| Obesity | 1 (5.3) | 4 (25.0) | 5 (20.0) |

*Asian heritage, n=2; Cuban, Hispanic, Mexican, and central/South Asian heritage AND Native Hawaiian or other Pacific Islander, n=1 each. †Occurring in ≥20% of patients in any treatment arm. ‡Includes diabetes mellitus and type 2 diabetes mellitus.

### sUA control

- Immediately after the first dose of NASP, mean (SD) sUA levels dropped by 97.6% and 97.7% with HD and LD NASP, respectively, to 0.2 (0.00) mg/dL **(Figure 2)**
- sUA levels were maintained at <2 mg/dL throughout the study in patients remaining on NASP treatment, while mean sUA returned to >6 mg/dL in patients who came off treatment
  - Majority of patients who came off NASP did not transition to oral ULTs
- In placebo-treated patients, mean sUA remained consistently similar to baseline values throughout the study

**Figure 2. Mean sUA over time in patients on (solid lines) or off (dashed lines) treatment (6D EE set)**

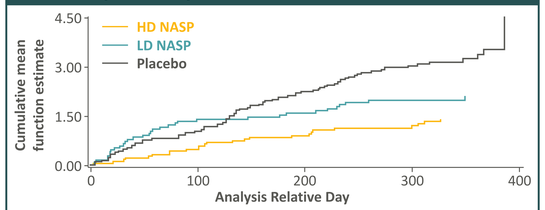



Off-trt defined as last dose + 28 days. Post-D measurements were taken 4.5 hours after infusion; no post-D measurements were collected for patients that were off treatment. Data for Pre-D measurements not shown. *7 days prior to next D. The n table counts summarize the number of non-missing assessments at each visit.

### Gout flares

- Overall, patients on HD NASP maintained a lower cumulative mean number of gout flares than placebo throughout the 48-week study (**Figure 3**)
- Patients on LD NASP had a greater cumulative flare rate than placebo during the first 12–16 weeks, which fell below placebo as the study continued and remained lower throughout the extension
- Over the study, the proportion of patients with ≥1 gout flare decreased in the NASP groups; during Weeks 1–4, flares occurred in 15.8% of patients on HD NASP, 43.8% on LD NASP, and 28.0% on placebo.
- During Weeks 21–24, flares occurred in 5.3% of patients on HD NASP, 12.5% on LD NASP, and remained at 28.0% on placebo
- During Weeks 45–48, 0% of patients on HD NASP and 7.7% on LD NASP experienced ≥1 flare compared to 22.7% on placebo

**Figure 3. Cumulative gout flare exposure over time while on treatment (6D EE set)**




Patients were censored at the end of treatment.

### Safety

- 6 patients on HD NASP, 4 on LD NASP and 4 on placebo discontinued treatment in Weeks 25–48. No new safety signals were reported[3]
- Most patients in both groups experienced only mild and moderate TEAEs
- Frequencies of selected AESIs are reported in **Table 2**
  - No infusion reaction within 1 hour were reported in the extension phase
  - All events of stomatitis were mild in severity, and resolved without medical intervention

**Table 2. Treatment-emergent adverse events, W1–48 (6D EE set, N=60)**

| | HD NASP (N=19) | LD NASP (N=16) | Placebo (N=25) |
|---|---|---|---|
| ≥1 TEAE, n (%) | 14 (73.7) | 14 (87.5) | 21 (84.0) |
| **Selected AESIs, n (%)** | | | |
| Gout flare | 9 (47.4) | 12 (75.0) | 17 (68.0) |
| Hypertriglyceridemia | 2 (10.5) | 1 (6.3) | 1 (4.0) |
| Infections and infestations | 8 (42.1) | 7 (43.8) | 5 (20.0) |
| COVID-19* | 3 (15.8) | 4 (25.0) | 1 (4.0) |
| Stomatitis† | 2 (10.5) | 3 (18.8) | 0 |
| Infusion-related reaction within 24 h | 2 (10.5) | 3 (18.8) | 1 (4.0) |
| Leukopenia | 0 | 1 (6.3) | 0 |
| Deep vein thrombosis | 0 | 0 | 1 (4.0) |

*No other infections occurred in >10% of patients in any arm. †Including mouth ulcers and aphthous ulcers.

**References:** **1.** Dalbeth N, et al. *Nat Rev Dis Primers* 2019;5:69; **2.** Tabi-Amponsah AD, et al. *Ann Rheum Dis* 2025; doi: 10.1016/j.ard.2025.05.017; online ahead of print; **3.** Baraf H, et al. EULAR 2024; Poster POS0260, Vienna, Austria; **4.** Gaffo A, et al. CCR East 2025, Poster, Destin, FL,USA; **5.** Baraf H, et al. CCR East, Poster, Destin, FL, USA

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**Abbreviations:** AESI, adverse event of special interest; BMI, body mass index; D, dose; EE, extension evaluable; eGFR, estimated glomerular filtration rate; H/HD, high-dose; IV, intravenous; L/LD, low-dose; n, number; NA, not applicable; NASP, nanoencapsulated sirolimus plus pegadricase; R, randomization; S, saline; SD, standard deviation; sUA, serum uric acid; TEAE, treatment-emergent adverse event; trt, treatment; ULT, urate-lowering therapy; W, week.