NASP and Uncontrolled Gout

Conference call for investors and analysts

September 16, 2025

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Agenda

Introduction and agenda

Guido Oelkers
Chief Executive Officer, Sobi

The painful burden of uncontrolled gout

Herbert S. B. Baraf, MD, FACP, MACR
Clinical Professor of Medicine, George Washington University
Associate Clinical Professor, University of Maryland
Senior Clinical Advisor, National Institutes of Health, NIAMS

NASP clinical program: A new era in uricase therapy

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Unlocking NASP's potential for patients with uncontrolled gout

Guido Oelkers
Chief Executive Officer, Sobi

Summary & Q&A

NIAMS, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Executive summary

The burden of uncontrolled gout[1-4]

- Uncontrolled gout affects a small but significant set of gout patients and is marked by **severe pain**, **serious health complications**, and **increased risk of death**

Uricase therapy provides relief[5-8]

- Uricase therapy is **recommended** for the treatment of uncontrolled gout and provides **rapid** and **robust** symptom relief[5-8]

Uricase therapy is currently underutilized[9]

- Uricase therapy is **currently underutilized** and lacks significant penetration
- Despite this, current market exceeds **$1 billion USD**[9]

NASP: An innovative solution to uricase therapy[10-14]

- **NASP** is an investigational but novel, **monthly,** two-component sequential uricase therapy without oral systemic immunosuppression
- **Rapid** and **sustained, significant** sUA reduction, while alleviating the **most debilitating** of symptoms

NASP, nanoencapsulated sirolimus plus pegadricase; sUA, serum uric acid; USD, United States dollar.

References: 1. Dalbeth N, et al. *Nat Rev Dis Primers.* 2019;5(1):69. **2.** Fels E, Sundy JS. *Curr Opin Rheumatol.* 2008;20(2):198-202. **3.** Vincent ZL, et al. *J Rheumatol.* 2017;44(3):368-373. **4.** Zuo T, et al. *BMC Cardiovasc Disord.* 2016;16(1):207. **5.** Richette P, et al. *Ann Rheum Dis.* 2017;76(1):29-42. **6.** Fitzgerald JD, et al. *Arthritis Rheumatol.* 2020;72(6):879-895. **7.** Schlesinger N, et al. *Nat Rev Rheumatol.* 2023;19(10):640-649. **8.** Dalbeth N, et al. *Lancet.* 2021;397(10287):1843-1855. **9.** Sobi internal market research. **10.** Kivitz A, et al. *Rheumatol Ther.* 2023;10(4):825. **11.** Baraf HSB, et al. The *Rheumatology (Oxford).* 2024;63(4):1058-1067. **12.** Sobi data on file. **13.** Baraf HSB, et al. Poster or Paper presented at: Florida Society of Rheumatology Annual Meeting; June 19–22, 2025; Lake Buena Vista, FL, USA. **14.** Strand V, et al. Poster or Paper presented at: American College of Rheumatology Convergence; November 14–19, 2024; Washington, DC, USA.

The painful burden of uncontrolled gout (UG)

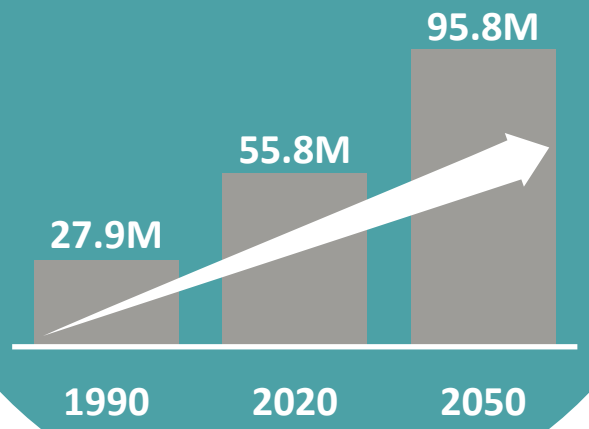
Herbert S. B. Baraf, MD, FACP, MACR
Clinical Professor of Medicine, George Washington University
Associate Clinical Professor, University of Maryland
Senior Clinical Advisor, National Institutes of Health, NIAMS

NIAMS, National Institute of Arthritis and Musculoskeletal and Skin Diseases.

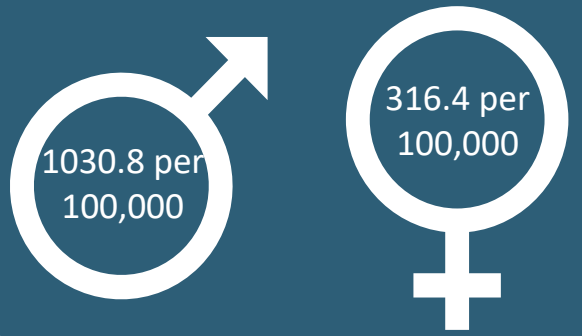
Gout – Increasing prevalence affects millions globally[1]

Gout is a chronic inflammatory disease caused by urate crystal buildup[2-4]

The global prevalence of gout nearly doubles every 30 years[1]



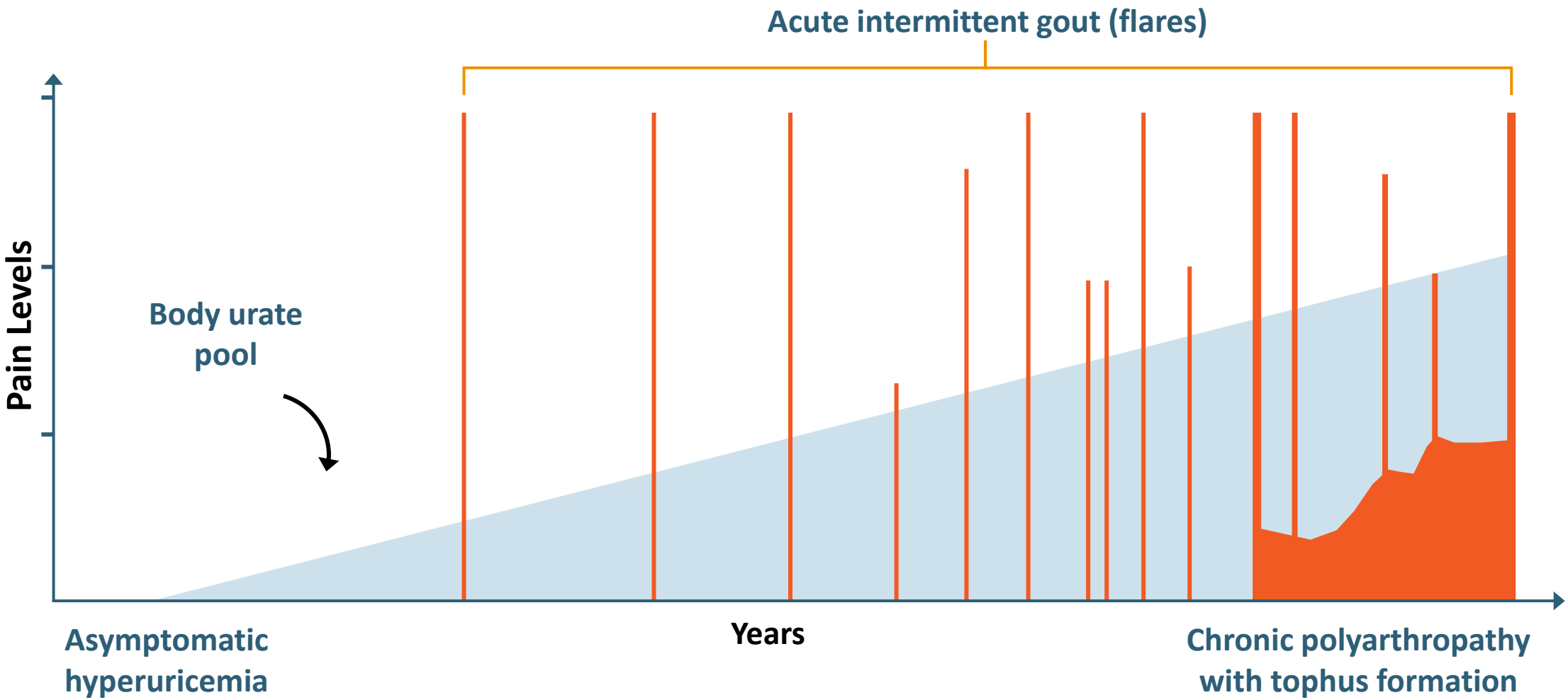
The global prevalence of gout is 3.2x higher in males than females and increases with age[1]



M, million.

References: 1. GBD 2021 Gout Collaborators. *Lancet Rheumatol.* 2024;6(8):e507-e517. **2.** An J, et al. *J Rheumatol.* 2024;51(9):848-861. **3.** Dalbeth N, et al. *Lancet.* 2021;397(10287):1843-1855. **4.** Timsans J, et al. *J Clin Med*. 2024;13(24):7616.

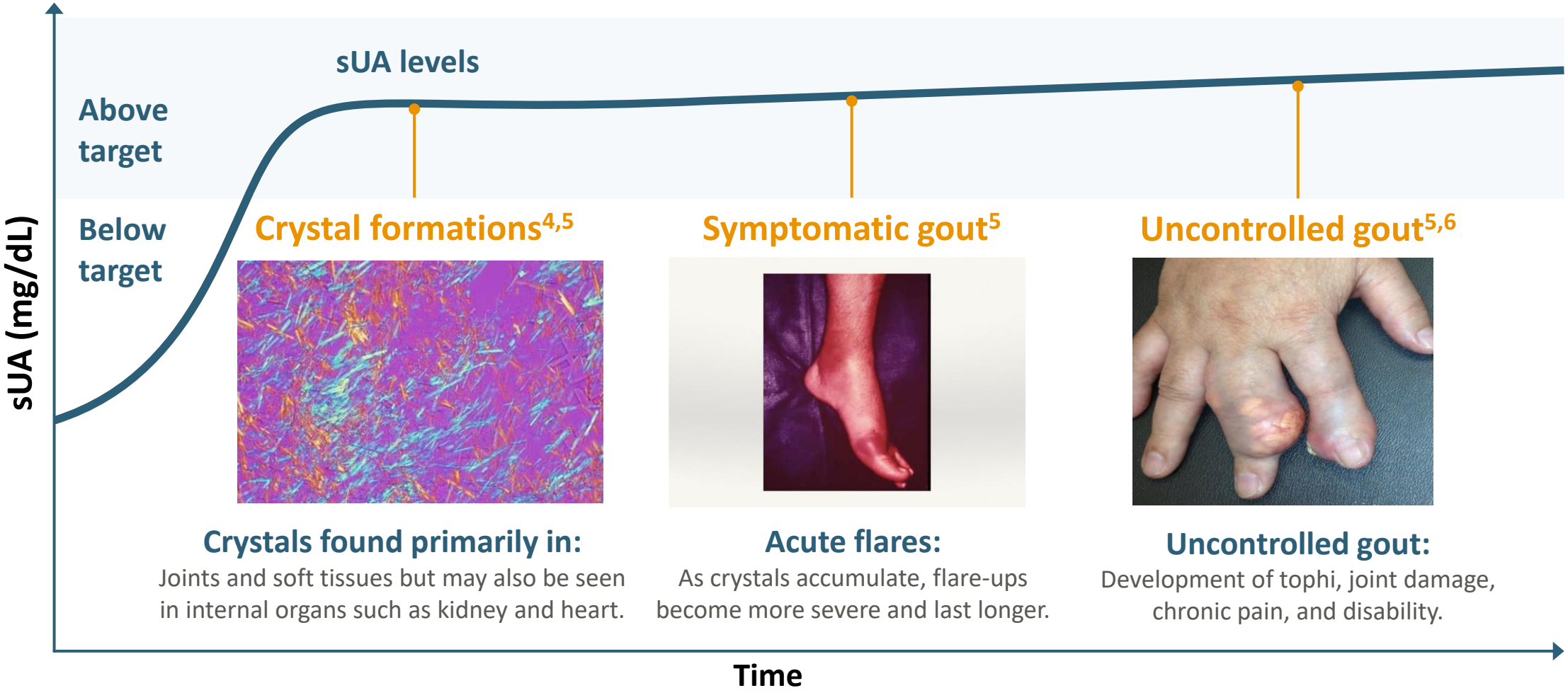
Gout – A severely impacted subset develop UG[1-3]



UG, uncontrolled gout.
Schematic representation adapted from Edwards NL. *Primer on the Rheumatic Diseases* 2008.[4]

References: 1. Richette P, Garay R. *Expert Opin Drug Discov*. 2013;8(2):183-189. **2.** Dave AJ, et al. *Expert Rev Clin Pharmacol.* 2012;5(5):501-508. **3.** Edwards NL. *Arthritis Rheum.* 2008;58(9):2587-2590.
4. Edwards NL. *Primer on Rheumatic Diseases.* 13th ed. Springer; 2008:241-249.

Gout – A severely impacted subset develop UG[1-3]



sUA, serum uric acid; UG, uncontrolled gout.

References: 1. Richette P, Garay R. *Expert Opin Drug Discov*. 2013;8(2):183-189. **2.** Dave AJ, et al. *Expert Rev Clin Pharmacol.* 2012;5(5):501-508. **3.** Edwards NL. *Arthritis Rheum.* 2008;58(9):2587-2590. **4.** Khanna P, et al. *J Clin Med.* 2020;9(10):3204. **5.** Dalbeth N, et al. *Nat Rev Dis Primers.* 2019;5(1):69. **6.** Fels E, Sundy JS. *Curr Opin Rheumatol*. 2008;20(2):198-202.

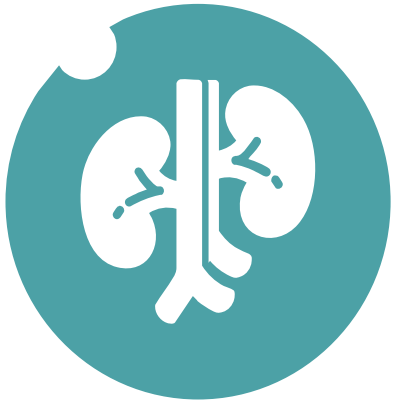
UG – Systemic inflammation may impact the whole body[1-3]

Cardiovascular Disease

1.5x higher risk
of **heart disease**[1]

Metabolic Syndrome

1.2x higher risk
of **diabetes**[1]



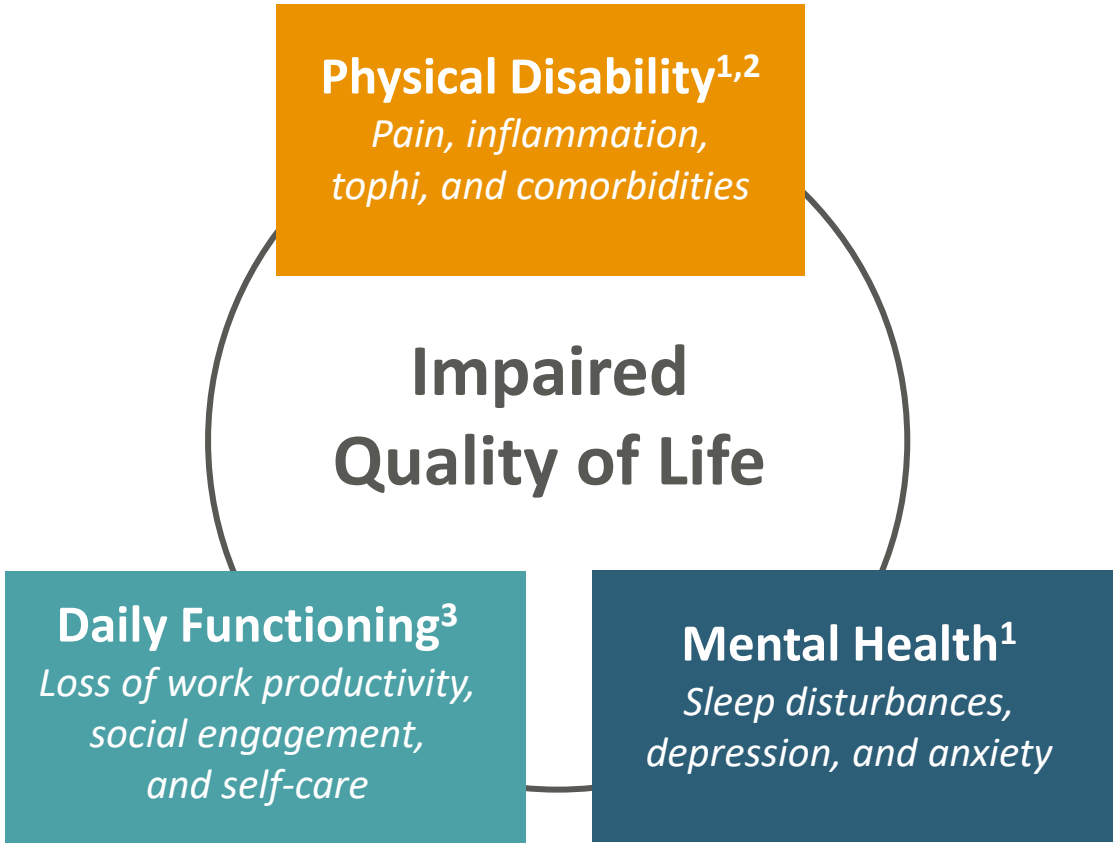
Chronic Kidney Disease (CKD)

2x higher risk
of **CKD**[1]

CKD, chronic kidney disease; sUA, serum uric acid; UG, uncontrolled gout.

References: 1. Francis-Sedlak M, et al. *Rheumatol Ther.* 2021;8(1):183-197. **2.** Vincent ZL, et al. *J Rheumatol.* 2017;44(3):368-373. **3.** Zuo T, et al. *BMC Cardiovasc Disord*. 2016;16(1):207.

UG – Chronic flares disrupt life and impact well-being



> *It's hard to relax, **I never know when a flare could happen."***
>
> *— Patient, France*

> *Gout stops me from doing **everything, apart from sitting down** which is all you can do."*
>
> *— Patient, UK*

> *Gout makes me feel helpless. I once had both hands swollen. I couldn't even pick up a toothbrush or a pencil. **I felt useless, I had to depend on my wife for everything."***
>
> *— Patient, US*

UG, uncontrolled gout; UK, United Kingdom; US, United States.

References: 1. Edwards NL. *Primer on Rheumatic Diseases.* 13th ed. Springer; 2008:241-249. **2.** Stewart S, et al. *Semin Arthritis Rheum.* 2020;50(4):805-811. **3.** Edwards NL, et al. *J Med Econ.* 2011; 2011;14(1):10-15.

Uricase treatment – Meeting the unmet need in UG[1-4]

The goal of treatment is to decrease gout flare frequency, reduce tophi, and **improve the quality of life** for patient through a **durable reduction in sUA** to <6 mg/dL.

First-line therapy[1,2]

Xanthine oxidase inhibitors

- Allopurinol and/or febuxostat

Second-line therapy[3,4]

Uricosurics

- Probenecid

Third-line therapy[3,4]

Uricases

- Pegloticase

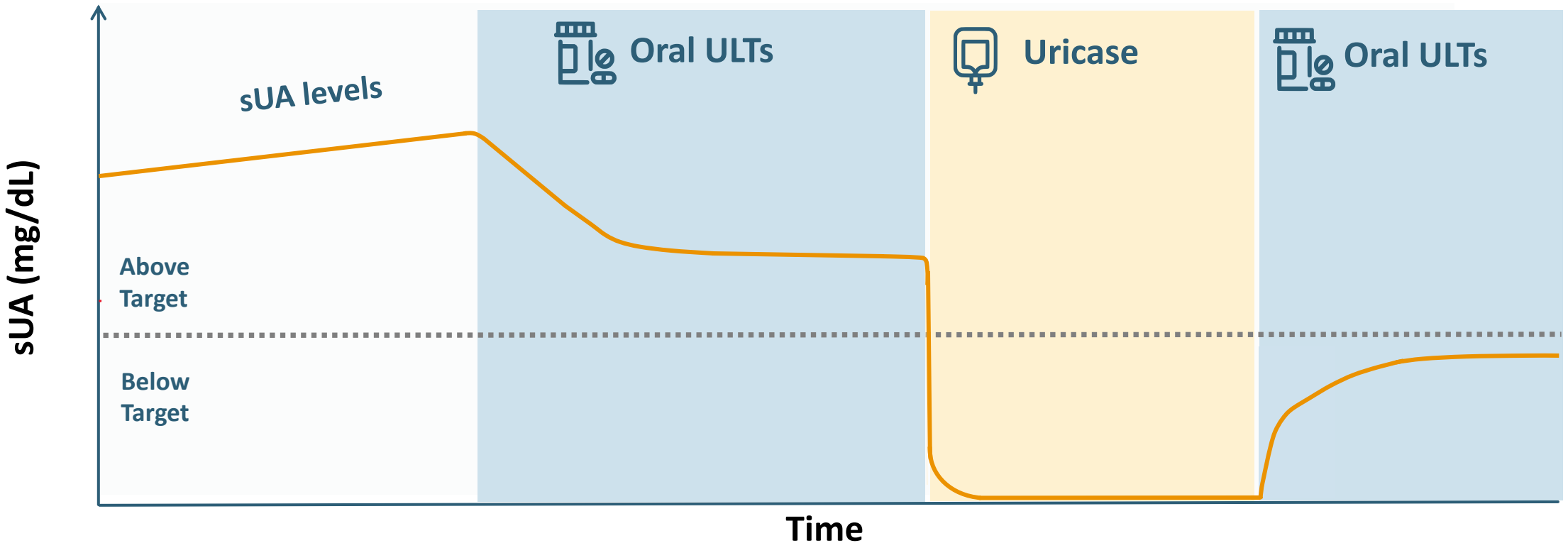
European Alliance of Associations for Rheumatology and
American College of Rheumatology Guideline for the Management of Gout:
Recommend uricase therapy for the treatment of UG[3,4]

sUA, serum uric acid; UG, uncontrolled gout..

References: 1. Arthritis Foundation. Treatments for gout. Updated June 10, 2022. Accessed August 2025. www.arthritis.org/health-wellness/treatment/treatment-plan/disease-management/treatments-for-gout **2.** Kumar M, et al. *Drugs Aging.* 2021;38(7):545-557. **3.** Richette P, et al. *Ann Rheum Dis.* 2017;76(1):29-42. **4.** Fitzgerald JD, et al. *Arthritis Rheumatol.* 2020;72(6):879-895.

Uricase treatment – Rapid results, sustained relief[1-2]

Illustrative



Benefits of uricase therapy: Rapid reduction of sUA levels, faster tophus resolution, less joint pain, and improved quality of life[1,2]

sUA, serum uric acid; ULT, urate-lowering therapy.
Schematic representation of sUA levels and gout flares in a patient with uncontrolled gout treated with uricase therapy, adapted from Edwards NL. *Primer on the Rheumatic Diseases.* 2008.[3]
References: 1. Schlesinger N, et al. *Nat Rev Rheumatol.* 2023;19(10):640-649. **2.** Dalbeth N, et al. *Lancet*. 2021;397(10287):1843-1855. **3.** Edwards NL. *Primer on Rheumatic Diseases.* 13th ed. Springer; 2008:241-249.

Uricase treatment – Efficacious but underutilized

<5%

of eligible patients are currently receiving uricase therapy[1]

Key factors limiting uricase uptake by HCPs and patients

- **Safety concerns** about AEs including flares, infusion reactions, anaphylaxis, and loss of efficacy due to anti-drug antibodies (ADAs)[2]
- Reluctance to use **broad and systemic immunosuppression** needed to prevent ADAs[1]
- **Twice-monthly dosing and lab monitoring, and daily/weekly concomitant therapies** adds burden and logistical challenges[1]
- **Patient access** to specialist HCP and coverage[1]
- **Comorbidities**[1]

HCP, healthcare professional.

Reference: 1. Data on file. **2.** Schlesinger, N. Kaufmann, D. *Explor Musculoskeletal Dis.* 2024;2:461–472.

NASP clinical programme: A new era in uricase therapy

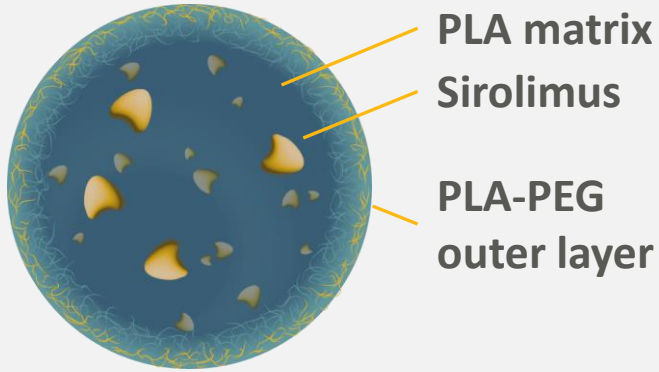
Rehan Azeem MBBS (MD), MPH

Medicine Development Leader—
Rheumatology & Specialty Care, Sobi

NASP – Targeted innovation in uricase therapy[1-4]

NASP is an investigational uricase therapy administered **every 4 weeks** through sequential infusion of **two components**.[1,2]

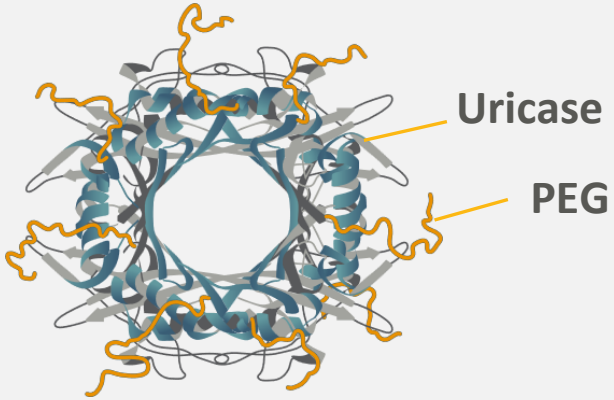
1



Nanoencapsulated Sirolimus[2-4]

Sirolimus induces targeted, antigen-specific tolerance to co-administered pegadricase.[3,4]

2



Pegadricase[1] **(Uricase)**

Methoxy-PEG-modified uricase reduces immune response and extends drug half-life.[1]

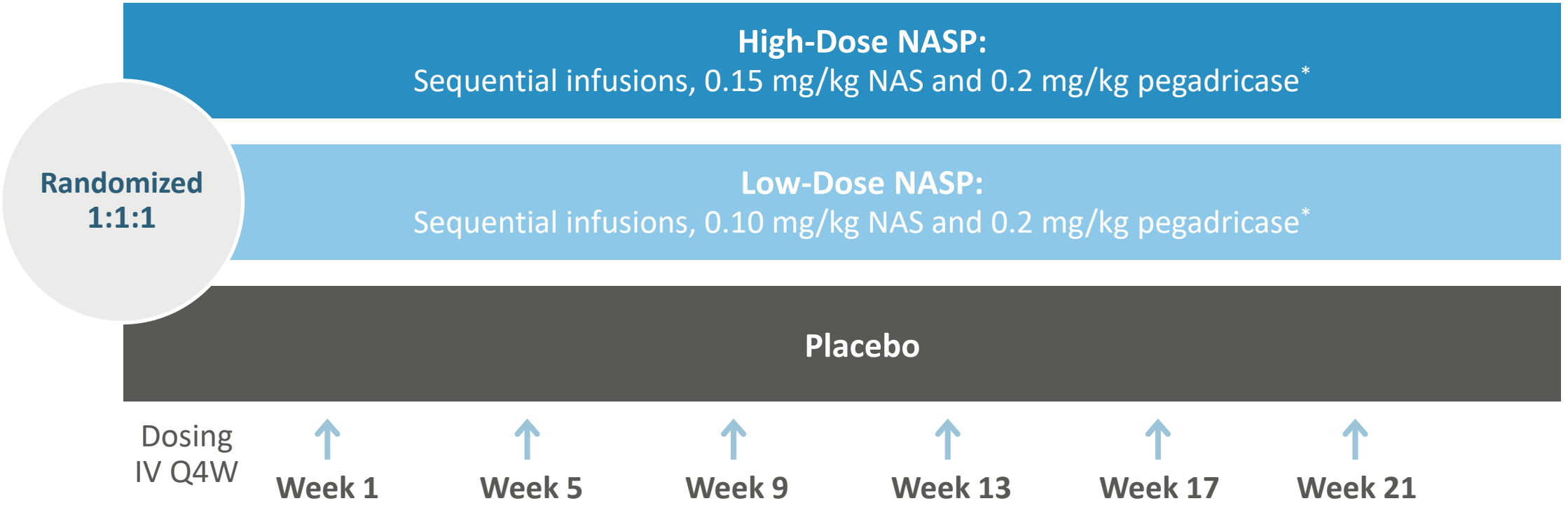
NASP, nanoencapsulated sirolimus plus pegadricase; PEG, polyethylene glycol; PLA, polylactic acid.

References: 1. Kivitz A, et al. *Rheumatol Ther.* 2023;10(4):825. **2.** Baraf HSB, et al. The *Rheumatology (Oxford)*. 2024;63(4):1058-1067. **3.** Kishimoto TK. *Front Immunol*. 2020;11:969. **4.** Sands E, et al. *Nat Commun.* 2022;13(1):272.

NASP – Protecting and powering uricase[1-8]

References: 1. Baraf HSB, et al. *Rheumatology (Oxford).* 2024;63(4):1058-1067. **2.** Garay RP, et al. *Expert Opin Drug Deliv*. 2012;9(11):1319-1323. **3.** Kishimoto TK. *Front Immunol.* 2020;11:969. **4.** Kivitz A, et al. *Rheumatol Ther*. 2023;10(4):825-847. **5.** Kivitz A, et al. Supplementary material. *Rheumatol Ther*. 2023;10(4):825-847. **6.** Sands E, et al. *Nat Commun*. 2022;13(1):272. **7.** Schlesinger N, et al. *Nat Rev Rheumatol*. 2023;19(10):640-649. **8.** Sherman M, et al. *Adv Drug Deliv Rev*. 2008;60(1):59-68.

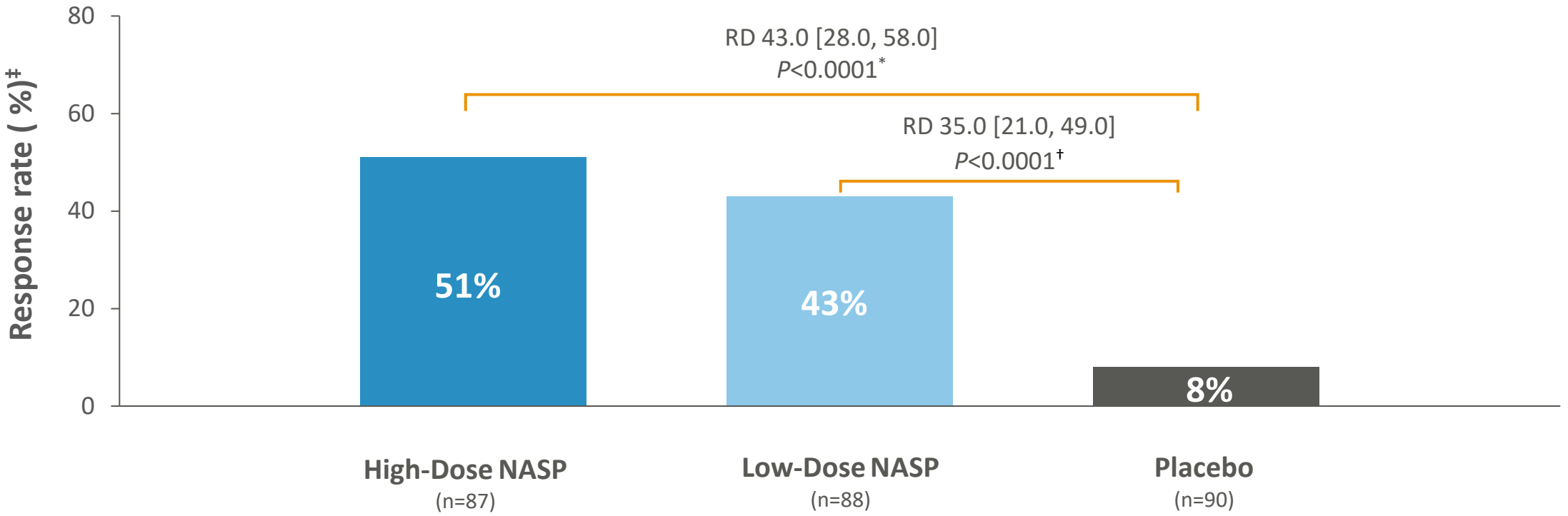
NASP – DISSOLVE I and II: Phase 3 trials in UG



Primary endpoint: Treatment response defined as maintaining sUA target for at least 80% of Weeks 21-24.

*Treatment was discontinued if the stopping rule was met: sUA <2.0 mg/dL 1 hour after infusion of the second component of the study drug during Week 1 and either sUA >1.0 mg/dL at the end of Week 3 or sUA >6.0 mg/dL at the end of any of Weeks 7, 11, 15, or 19. In the overall ITT population from DISSOLVE I and DISSOLVE II, the most common reasons for treatment discontinuation among patients who received NASP were meeting the stopping rule, adverse events, and withdrawal of consent. Patients received colchicine or a nonsteroidal anti-inflammatory drug for gout flare prophylaxis and premedication with prednisone, fexofenadine, and methylprednisolone for infusion reactions.
ITT, intent-to-treat; IV, intravenous; NAS, nanoencapsulated sirolimus; NASP, nanoencapsulated sirolimus plus pegadricase; Q4W, every 4 weeks; sUA, serum uric acid; UG, uncontrolled gout.
Reference: Baraf HSB, et al. Poster or Paper presented at: Florida Society of Rheumatology Annual Meeting; June 19–22, 2025; Lake Buena Vista, FL, USA.

NASP – Demonstrated significant sUA control vs placebo



Primary endpoint: Treatment response defined as maintaining sUA target for at least 80% of Weeks 21-24.

*RD vs placebo [97.5% CI] and p-value for each treatment group are indicated above the HD and LD columns. Missing response data in TP6 were multiple imputed. Mantel-Haenszel testing was performed with randomization stratum of tophus presence (y/n), where applicable, with a two-sided error rate α=2.5% for the two comparisons of study drug against placebo. † Two-sided Chi-square testing with a type 1 error rate alpha of 2.5% was applied to adjust for the two comparisons against placebo. ‡ Data shown are for pooled DISSOLVE I and II.

CI, confidence interval; HD, high-dose; LD, low-dose; NASP, nanoencapsulated sirolimus plus pegadricase; RD, risk difference; sUA, serum uric acid; TP, time point.

Reference: Baraf HSB, et al. EULAR 2024 European Congress of Rheumatology; June 12–15, 2024; Vienna, Austria.

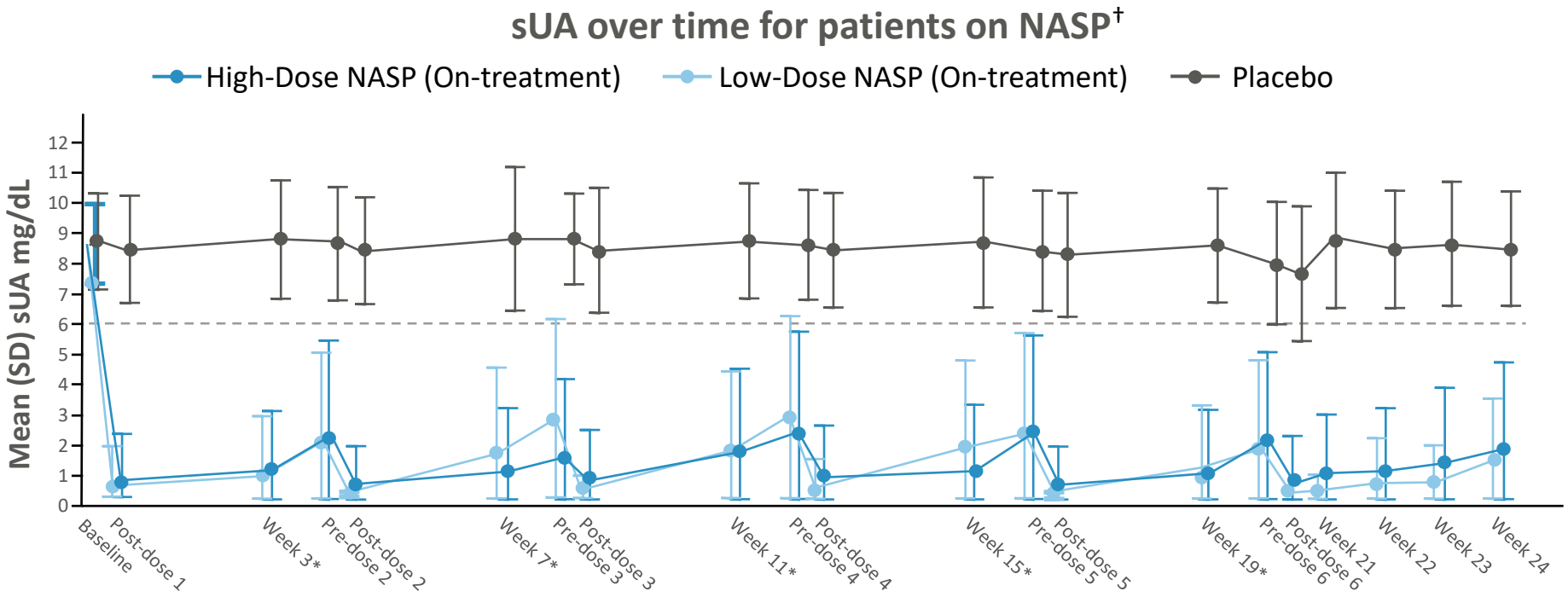
NASP – Immediate impact, maintained over 6 months

Mean sUA reduction from baseline to 1 hour post first infusion:

94%
on high-dose NASP

95%
on low-dose NASP

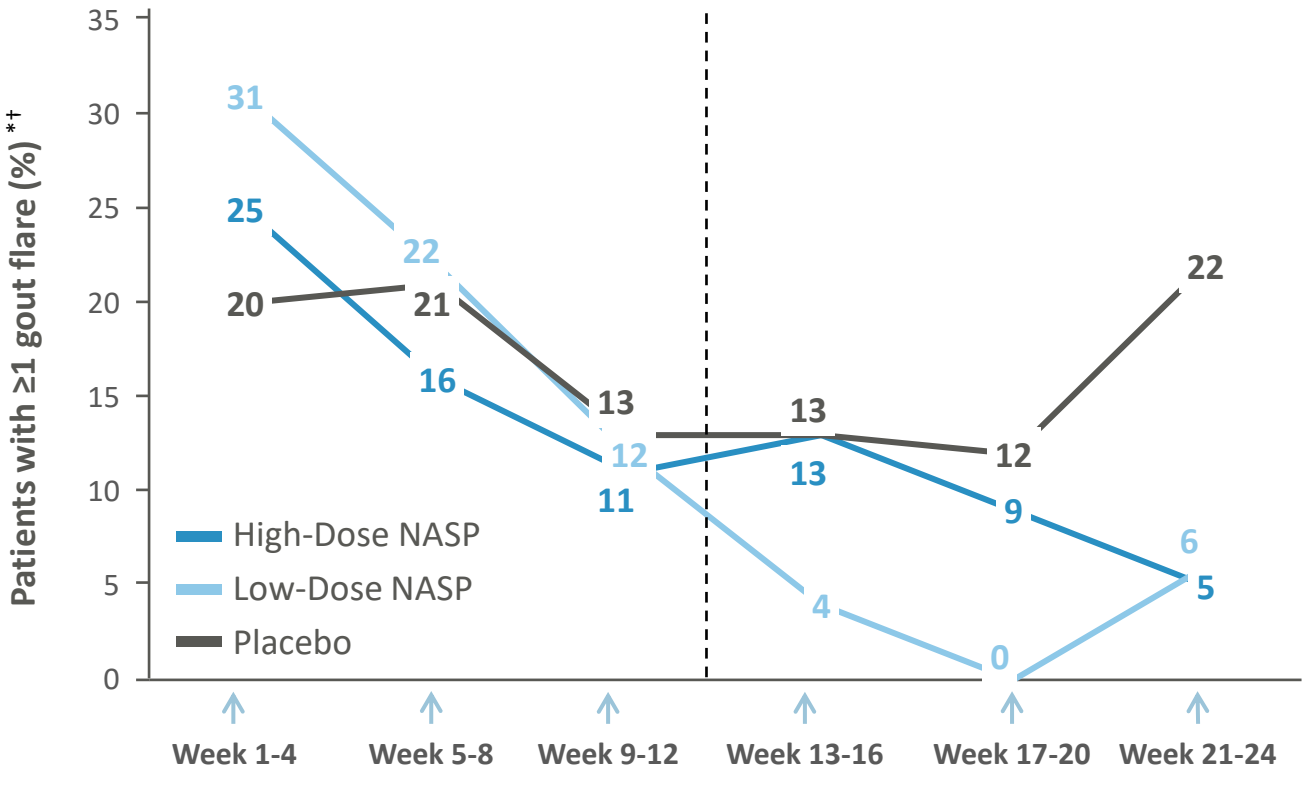
vs 3% on placebo



sUA levels decreased after the **first administration** of NASP and were **maintained** throughout the 6-month treatment period.

*Data shown are for pooled DISSOLVE I and II for patients on treatment. †Post hoc analysis.
sUA, serum uric acid; NASP, nanoencapsulated sirolimus plus pegadricase.
Reference: Sobi data on file.

NASP – Reduced gout flares over course of treatment



WEEKS 1-12
SIMILAR GOUT FLARES RATES
NASP & PLACEBO

FLARE-FREE AFTER 6 DOSES
(Weeks 21-24)

95% on high-dose

94% on low-dose

> ***The biggest thing for me is not having any flares;***
> *that would be amazing.*

*Data shown are for pooled DISSOLVE I&II for patients on treatment. †Post-hoc analysis.
NASP, nanoencapsulated sirolimus plus pegadricase.
Reference: Sobi data on file.

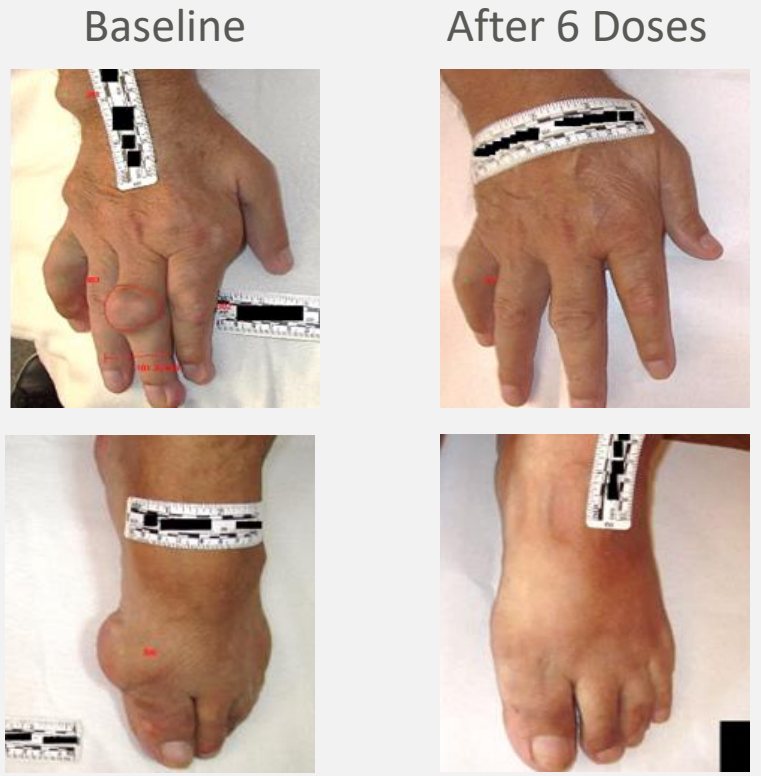
NASP – Positive resolution of tophi by Month 6

Complete tophus response*†

High-dose NASP	49%
Low-dose NASP	70%
Placebo	5%

~10-14 times complete resolution of tophi with high-dose and low-dose NASP vs placebo.

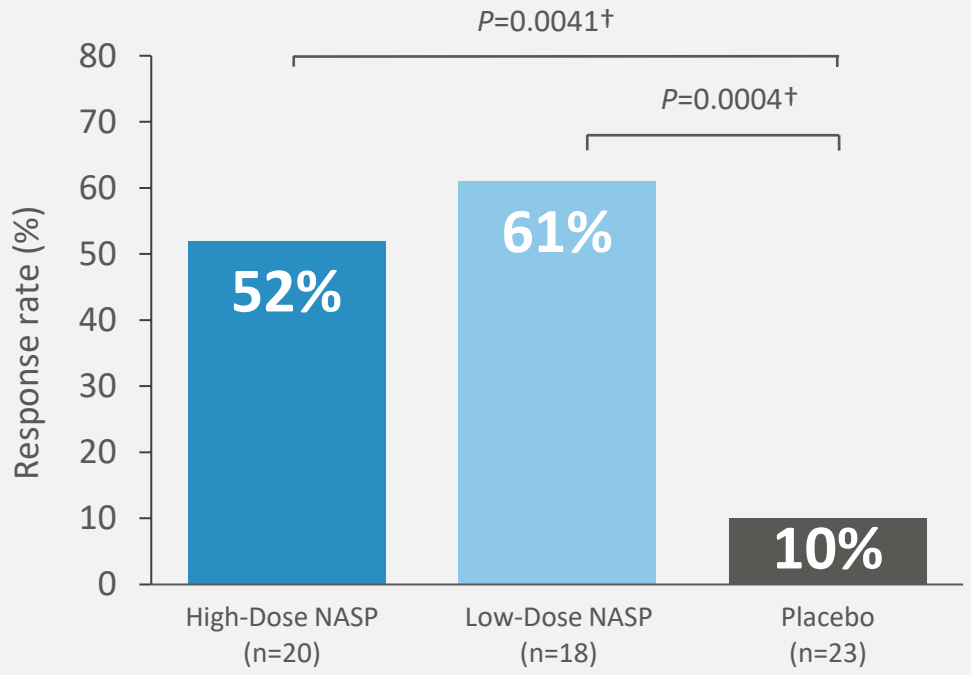
Complete response to treatment of high-dose NASP*†



*Complete response was defined as 100% reduction in the area or complete disappearance of a tophus without enlargement of any existing tophus and no new tophus. Tophi were considered measurable if they were ≥5 mm in the longest dimension at baseline and had borders distinguishable to the independent reader. †Post hoc analysis.
NASP, nanoencapsulated sirolimus plus pegadricase.
Reference: Baraf HSB, et al. Poster or Paper presented at: Florida Society of Rheumatology Annual Meeting; June 19–22, 2025; Lake Buena Vista, FL, USA.

NASP – Positive data in CKD Stage 3 patients[1]

52% and 61% of CKD Stage 3 patients receiving NASP achieved a 6-month sUA response[1*]



CKD Stage 3 patients receiving NASP had stable eGFR function[1*‡]

3.3 mL/min/1.73 m²
IMPROVEMENT on high-dose NASP

3.7 mL/min/1.73 m²
IMPROVEMENT on low-dose NASP

2.7 mL/min/1.73 m²
DECLINE on placebo

Patients with UG have a **twofold higher risk of developing CKD** than those with controlled gout.[2]

*Post hoc analysis. †*P*-values for each treatment group are based on RD (97.5% CI); RD (97.5% CI) values for pooled ITT population were: high dose vs placebo: 43% (28%, 58%); low dose vs placebo: 35% (21%, 49%); RD values for CKD stage 3 were: high dose vs placebo: 40% (9%, 72%); low dose vs placebo: 50% (18%, 81%). Missing response data in TP6 were multiple imputed. Mantel-Haenszel test was performed with randomization of tophus presence (yes/no) with a two-sided error rate of α=2.5% to account for the two comparisons of study drug against placebo. Response rate, defined as sUA levels <6 mg/dL for ≥80% of the time during TP6. Data shown are for pooled DISSOLVE I and II. ‡The baseline mean in the low dose group is skewed due to a single subject with an unusually high baseli
CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ITT, intent-to-treat; NASP, nanoencapsulated sirolimus plus pegadricase; RD, risk difference; sUA, serum uric acid; TP, time point; UG, uncontrolled gout.

References: **1.** Khanna P, et al. American Society of Nephrology Kidney Week 2024; October 23–26; San Diego, CA, USA. **2.** Francis-Sedlak M, et al. *Rheumatol Ther.* 2021;8(1):183-197.

NASP – A well tolerated therapy

Adverse Events of Special Interest*† (>5% of patients)	High-Dose NASP (N= 87)	Low-Dose NASP (N = 88)	Placebo (N=90)
Gout flares	42.5%	44.3%	43.3%
Infections (including viral)	23%	18.2%	16.7%
COVID-19 infection‡	*5.7%*	*5.7%*	*6.7%*
Hypertriglyceridemia¶	6.9%	4.5%	6.7%
Stomatitis§	9.2%	3.4%	0%
Infusion-related AEs (24h)	8%	6.8%	2.2%
Infusion reactions (1h.) inc. anaphylaxis#	*3.4%*	*4.5%*	*0%*

All instances of stomatitis were mild to moderate

No hospitalizations from anaphylaxis

No major renal, cardiovascular, or hepatic safety signals or risks were identified with NASP therapy.

*Safety data shown are during the first 6 treatment periods during DISSOLVE I and II. Events occurring during the extension phase of the DISSOLVE I study are excluded. † AESIs included in protocol as agreed with FDA; No other TEAEs ≥5%. ‡ There were no other individual infections >2%. ¶Dyslipidaemia/hypertriglyceridaemia/hyperlipidaemia. § Stomatitis/oral ulcer/aphthous ulcer; 67% mild, 33% moderate. # Infusion reactions (1h) are included in the infusion-related AEs (24h).
AE, adverse event; AESI, adverse reaction of special interest; COVID-19, coronavirus disease 2019; FDA, US Food and Drug Administration; NASP, nanoencapsulated sirolimus plus pegadricase; TEAE, treatment-emergent adverse event.
Reference: Baraf HSB et al. EULAR 2024 European Congress of Rheumatology; June 12–15, 2024; Vienna, Austria.

Unlocking NASP’s potential for patients with uncontrolled gout

Guido Oelkers
Chief Executive Officer, Sobi

Paving the way for NASP – From submission to launch

Key milestones:

NASP FDA BLA
Submission: June 2025

NASP FDA BLA
Review Process: Standard

Target PDUFA Date:
June 2026

Launch readiness activities:

1

Highlight
unmet needs and uricase underutilization

2

Strengthen
belief in NASP's efficacy and unique clinical profile

3

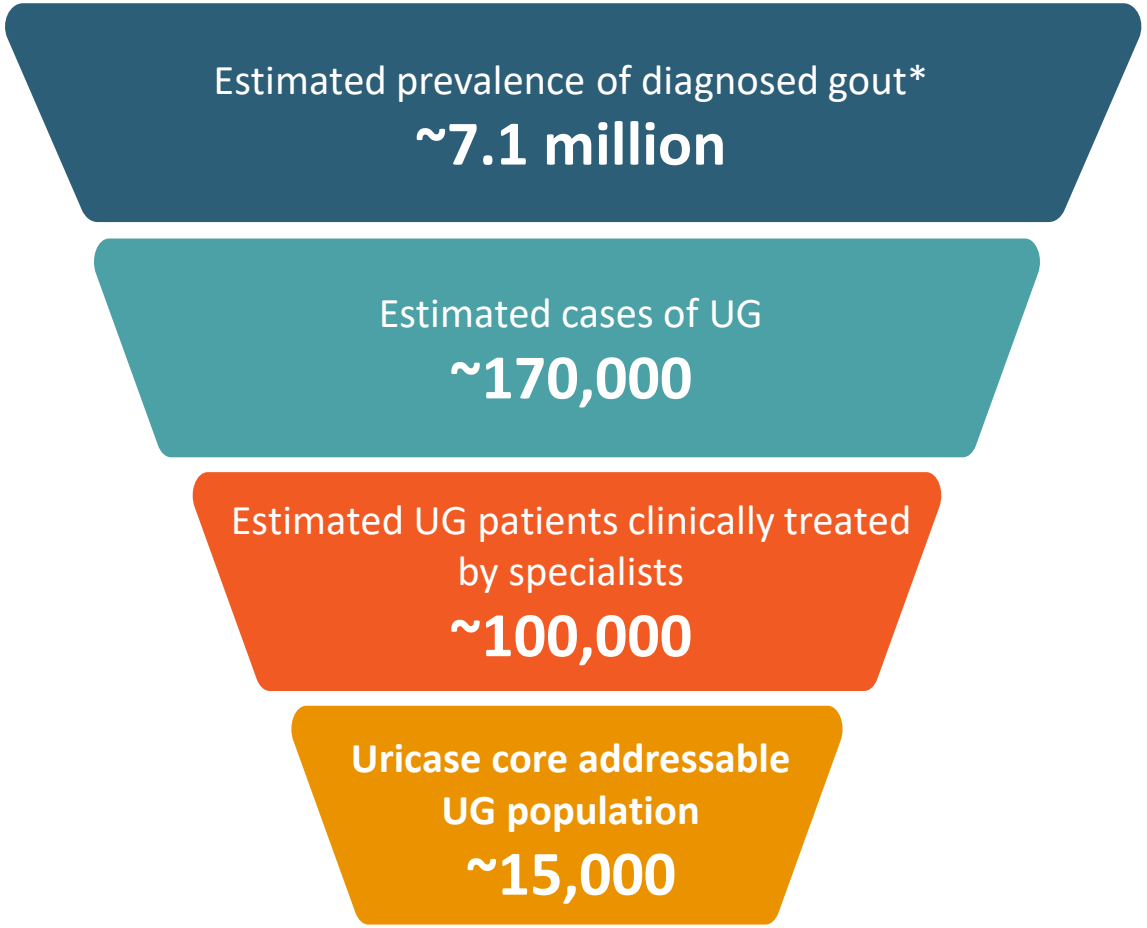
Mitigate
financial and logistical barriers to treatment

4

Optimize
customer, caregiver, and physician experience

BLA, Biologics License Application; FDA, Food and Drug Administration; NASP, nanoencapsulated sirolimus plus pegadricase; PDUFA, Prescription Drug User Fee Act.

Uricase treatment – A defined, high unmet need market with significant revenue potential[1-7]



Uricase therapy is currently underutilized and lacks significant penetration in the treatment of UG

Current UG market potential exceeds $1 billion USD and remains a growing market segment within gout

Large gout population funnels down to a **core addressable UG population of approximately 15K†**

*Of the estimated 9.7 million patient-reported prevalence of gout. All figures are from 2023.

†Core addressable UG population: 10K–20K patients.

UG, uncontrolled gout; USD, United States dollar.

References: 1. Chen-Xu M, et al. *Arthritis Rheumatol*. 2019;71(6):991-999. **2.** McAdams MA, et al. *J Rheumatol*. 2011;38(1):135-141. **3.** Choi HK, et al. *Arch Intern Med*. 2005;165(7):742-748. **4.** Roubenoff R, et al. *JAMA*. 1991;266(21):3004-3007. **5.** IQVIA LAAD Gout Claims data: % of uncontrolled gout patients (Sobi internal definition, all cohorts) seen by a Rheumatologist or Nephrologist in 2023. **6.** Internal Market Research, 2020 **7.** Internal Market Research, 2025.

NASP – Enhancing the profile to maximize possibilities

Robust lifecycle management plan initiated and underway

Enhance NASP product profile

Address unique needs of several uncontrolled gout special populations

Optimize patient and provider experience

Market expansion plans under evaluation

Significant opportunity exists in international markets for NASP

NASP, nanoencapsulated sirolimus plus pegadricase.

NASP – A key strategic growth driver for Sobi

Investments in 2025 for multiple launches in 2025/2026

2

Major launches

1. Altuvoct
2. Vonjo

3

Key filings

1. Gamifant: HLH/MAS
2. Aspaveli: C3G/IC-MPGN
3. **NASP: Uncontrolled gout**

4

Priority development projects in area of high unmet medical need

1. Gamifant: IDS
2. Vonjo: VEXAS
3. Vonjo: CMML
4. Altuvoct: Synovitis

C3G, C3 glomerulopathy; CMML, chronic myelomonocytic leukemia; HLH, hemophagocytic lymphohistiocytosis; IC-MPGN, immune complex membranoproliferative glomerulonephritis; IDS, interferon-gamma driven sepsis; MAS, macrophage activation syndrome; NASP, nanoencapsulated sirolimus plus pegadricase; VEXAS, vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic syndrome.

NASP – An investigational treatment designed for the safe and effective treatment of UG

Effective urate reduction[1,2]

- Shown to rapidly and significantly reduce sUA levels

Alleviation of symptoms[2-4]

- NASP treatment greatly reduced flares, shrank tophus size, and improved quality of life

Low treatment burden[5,6]

- Sequential infusion given monthly without the need for systemic immunosuppression[5,6]

Launch readiness

- Anticipated US launch Q2 2026
- Robust lifecycle management plan and significant opportunity in international markets

NASP, nanoencapsulated sirolimus plus pegadricase; Q2, quarter 2; sUA, serum uric acid; US, United States; UG, uncontrolled gout.

Reference: 1. Baraf HSB, et al. EULAR 2024 European Congress of Rheumatology; June 12–15, 2024; Vienna, Austria. **2.** Sobi data on file. **3.** Baraf HSB, et al. Poster or Paper presented at: Florida Society of Rheumatology Annual Meeting; June 19–22, 2025; Lake Buena Vista, FL, USA. **4.** Strand V, et al. Poster or Paper presented at: American College of Rheumatology Convergence; November 14–19, 2024; Washington, DC, USA. **5.** Kivitz A, et al. *Rheumatol Ther.* 2023;10(4):825. **6.** Baraf HSB, et al. The *Rheumatology (Oxford)*. 2024;63(4):1058-1067.


Q&A