SAFETY & EFFICACY OF SEL-212 IN PATIENTS WITH GOUT REFRACTORY TO CONVENTIONAL TREATMENT: OUTCOMES FROM TWO RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, MULTICENTER PHASE III STUDIES

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Disclosures

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Picture taking is **ALLOWED** during my presentation (including presented slides)
Patients with refractory gout have limited effective therapeutic options

- **ACR 2020 guidelines “strongly recommend”** uricase-based therapy for gout patients who:
  - “have failed to achieve uric acid lowering targets” 
    AND  
  - “continue to have frequent gout flares...” 
    OR  
  - “...nonresolving tophi”

- Uricase-based therapy is effective for refractory gout but: “comes with ..., twice-monthly infusions, and the potential for serious allergic reactions”

- Immunogenicity of the one US-approved uricase-based treatment can impair efficacy and increase the incidence of infusion reactions
  - May contribute to the 29-58% treatment failure rate with uricase therapy

- This presentation includes top line data from DISSOLVE Phase 3 studies of SEL-212, which is being explored as a potential new uricase-based therapy

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SEL-212 is a monthly 2-component infusion therapy designed to treat refractory gout

- Pegadricase (SEL-037) is a potent pegylated uricase that converts uric acid to soluble and readily excreted allantoin$^{1,2}$
- Pegadricase, like most uricases, elicits a vigorous ADA response, limiting its use as a monotherapy$^2$
- SEL-110, an immune-tolerizing nanoencapsulated rapamycin, administered 30 minutes before pegadricase, has demonstrated dose dependent inhibition of anti-pegadricase antibodies in phase 1 and phase 2 trials$^{1,2}$
- SEL-212 is the combination of the sequential infusion of these 2 components

ADA, anti-drug antibodies; sUA, serum uric acid
DISSOLVE I & II study design: Two replicate, double blind, placebo-controlled trials

Participants were:

<table>
<thead>
<tr>
<th>Arm</th>
<th>SEL-110 Dose</th>
<th>SEL-037 Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEL-212 High dose</td>
<td>0.15 mg/kg</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td>SEL-212 Low dose</td>
<td>0.1 mg/kg</td>
<td>0.2 mg/kg</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Allocated into 3 study arms, randomized 1:1:1

Administered sequential infusions every 28 days

- Treatment arms differed in the dose level of SEL-110 (0.15 vs 0.1 mg/kg)
- Patients in both treatment arms received 0.2 mg/kg of pegadricase (SEL-037)
- Placebo patients received sequential infusions of saline
- Prophylaxis against infusion reactions and gout flares were given to all participants
DISSOLVE I & II study design

Primary Efficacy Endpoint
sUA < 6 mg/dL for at least 80% of the time (0h, ~4.5h, and days 7, 14, 21 and 28) during month 6 of treatment (TP6)

Baseline

6-Month Safety Extension (Blinded)

DISSOLVE I (US Study)
29 sites in US
- 0.15 SEL-212 (High dose, n=38)
- 0.1 SEL-212 (Low dose, n=37)
- Placebo (n=37)

DISSOLVE II (Global Study)
37 sites in US, Russia, Ukraine, Georgia, and Serbia
- 0.15 SEL-212 (High dose, n=49)
- 0.1 SEL-212 (Low dose, n=51)
- Placebo (n=53)

Dosing Day
TP1 TP2 TP3 TP4 TP5 TP6 TP7 TP8 TP9 TP10 TP11 TP12
- 28 days

IV, intravenous; sUA, serum uric acid; TP, treatment period
DISSOLVE I & II study design: Participant selection

Key inclusion criteria

- Adults with history of symptomatic gout
  - ≥3 gout flares within 18 months prior to screening, OR
  - or ≥1 tophus, OR
  - current diagnosis of gouty arthritis
- History of chronic refractory gout:
  - Failure to normalize sUA and control symptoms with any xanthine oxidase inhibitor
  - Screening sUA ≥7 mg/dL

Key exclusion criteria

- History of anaphylaxis, severe allergic reactions, or severe atopy
- Allergy to PEGylated products
- Requires drugs known to interact with rapamycin
- Uncontrolled diabetes or hypertension
- Unstable cardiovascular/cerebrovascular disease or congestive heart failure (NY Heart Association Class III or IV)
- Prior exposure to experimental or marketed uricase therapy
- G6PD deficiency

Stringent stopping rules were implemented to minimize the risk of infusion related adverse events
Subject flow

**DISSOLVE I**
(US Study)

- SCREENED: 413
  - 15 re-screened
  - 298 initially screen failed
- RANDOMIZED: 115
  - 3 not dosed (subsequently screen failed)
- RANDOMIZED & DOSED: 112
  - High Dose 0.15 SEL-212: 38
  - Low Dose 0.10 SEL-212: 37
  - Placebo: 37

**DISSOLVE II**
(Global Study)

- SCREENED: 486
  - 17 re-screened
  - 328 initially screen failed
- RANDOMIZED: 158
  - 5 not dosed (subsequently screen failed)
- RANDOMIZED & DOSED: 153
  - High Dose 0.15 SEL-212: 49
  - Low Dose 0.10 SEL-212: 51
  - Placebo: 53

**Intention to Treat**

- ITT, intention to treat

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## Baseline demographics

<table>
<thead>
<tr>
<th></th>
<th>DISSOLVE I (US Study)</th>
<th>DISSOLVE II (Global Study)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High dose (38)</td>
<td>Low dose (37)</td>
</tr>
<tr>
<td><strong>Age in years, mean (SD)</strong></td>
<td>54 (12)</td>
<td>55 (10.6)</td>
</tr>
<tr>
<td><strong>Age ≥50 years, %</strong></td>
<td>66</td>
<td>73</td>
</tr>
<tr>
<td><strong>BMI, mean (SD)(kg/m²)</strong></td>
<td>35 (6.4)</td>
<td>34 (7.5)</td>
</tr>
<tr>
<td><strong>Gender, %</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>92</td>
<td>95</td>
</tr>
<tr>
<td><strong>Race, %</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>71</td>
<td>76</td>
</tr>
<tr>
<td><strong>Region, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>38 (100)</td>
<td>37 (100)</td>
</tr>
<tr>
<td>Russia, Ukraine, Serbia, Georgia</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

- Balanced for age, BMI, and sex across treatment groups in both studies
- Racial imbalances were noted in both studies
- ~15% of DISSOLVE II patients were from Russia and Ukraine
### Disease characteristics

Data are represented as mean (standard deviation) unless otherwise stated.

<table>
<thead>
<tr>
<th></th>
<th>DISSOLVE I (US Study)</th>
<th>DISSOLVE II (Global Study)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High dose (38)</td>
<td>Low dose (37)</td>
</tr>
<tr>
<td>Duration of gout diagnosis, years</td>
<td>14.3 (10.5)</td>
<td>11.9 (10.0)</td>
</tr>
<tr>
<td></td>
<td>High dose (49)</td>
<td>Low dose (51)</td>
</tr>
<tr>
<td>Participants with tophi at baseline: n (%)</td>
<td>22 (57.9)</td>
<td>21 (56.8)</td>
</tr>
<tr>
<td>sUA (mg/dL)</td>
<td>8.7 (1.4)</td>
<td>8.2 (1.9)</td>
</tr>
<tr>
<td></td>
<td>High dose (11.6)</td>
<td>Low dose (11.1)</td>
</tr>
<tr>
<td>Tender joints</td>
<td>1.9 (5.1)</td>
<td>3.5 (6.4)</td>
</tr>
<tr>
<td></td>
<td>11.6 (11.5)</td>
<td>11.1 (12.8)</td>
</tr>
<tr>
<td>Swollen joints</td>
<td>2.0 (4.3)</td>
<td>3.6 (7.5)</td>
</tr>
<tr>
<td></td>
<td>6.9 (10.4)</td>
<td>4.4 (8.1)</td>
</tr>
</tbody>
</table>

- Gout severity was numerically greater in **DISSOLVE II** as evidenced by a higher baseline incidence of tophi, tender joints and swollen joints.
Primary endpoint: Response to SEL-212 versus placebo

Primary efficacy endpoints were met for both studies and doses

- In the high dose group, 56% and 46% of patients responded to treatment in DISSOLVE I & II, respectively
- In the low dose group, 48% and 40% of patients responded to treatment in DISSOLVE I & II, respectively

CI, confidence interval of the risk difference

1Responders were defined as subjects with sUA levels <6mg/dL for at least 80% of the time during month 6 of therapy (TP6). Subjects who dropped from study due to 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.

2Difference vs placebo (97.5% CI) and p-value versus placebo group for each treatment group are indicated above each bracket
SEL-212 versus placebo in patients aged ≥50 years

- A pre-specified subanalysis of patients aged ≥50 years showed response rates\(^1\) of 65% and 47% in the high dose group for the US & Global Studies, respectively.

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\(^1\)Responders were defined as subjects with sUA levels <6mg/dL for at least 80% of the time during month 6 of therapy (TP6). Subjects who dropped from study due to 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.

\(^2\)Difference vs placebo [97.5% CI] and p-value versus placebo group for each treatment group are indicated above each bracket.
Significant reduction of serum uric acid from baseline to TP6

**Absolute change in sUA**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean sUA Δ from BL to TP6 (mg/dL, SE)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISSOLVE I (US)</td>
<td>-5.3 (-5.2)</td>
<td>p&lt;0.001²</td>
</tr>
<tr>
<td>DISSOLVE II (Global)</td>
<td>-5.1 (-4.3)</td>
<td>p&lt;0.001²</td>
</tr>
</tbody>
</table>

**Mean % change in sUA**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean % sUA Δ from BL to TP6 (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISSOLVE I (US)</td>
<td>-62.3 (-58.3)</td>
<td>p&lt;0.001²</td>
</tr>
<tr>
<td>DISSOLVE II (Global)</td>
<td>-58.1 (-52.2)</td>
<td>p&lt;0.001²</td>
</tr>
</tbody>
</table>

**Median % change in sUA**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median % change in sUA (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISSOLVE I (US)</td>
<td>-96.9</td>
<td></td>
</tr>
<tr>
<td>DISSOLVE II (Global)</td>
<td>-79.5</td>
<td></td>
</tr>
</tbody>
</table>

- Significant reductions in sUA were observed for all treatment groups compared to placebo
- Analyses include all available patient data, including those withdrawn from treatment
- Median % change estimates indicate very large reductions in at least half of patients
- Analyses of secondary endpoints are ongoing

BL, baseline; sUA, serum uric acid; TP, treatment period

¹Reduction of mean sUA as computed by subtracting the Baseline (BL) sUA level from the mean sUA during Treatment Period 6 (TP6) defined as the area under the time curve divided by the corresponding time interval.

²Analysis using ANCOVA model with reduction or percent reduction of mean sUA at TP6 from baseline as dependent variable and randomization stratum and baseline sUA as covariates. Missing values of change or percent change from baseline were multiple imputed by using the Recursively Partitioned Mixture Model. The means of treatment groups are pooled estimates after multiple imputation and 2-sided p-values.

³Percent reduction mean sUA as computed by subtracting Baseline (BL) sUA level from the mean sUA during TP6 divided by the Baseline and reported as either absolute difference or percent difference.
## All Adverse Events of Special Interest (AESI)\(^1\)

### Pooled Studies at 6-Month Primary Endpoint

<table>
<thead>
<tr>
<th>Safety Set</th>
<th>High dose (87) n (%)</th>
<th>Low dose (88) n (%)</th>
<th>Placebo (90) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥1 Treatment-emergent AESI</td>
<td>55 (63.2)</td>
<td>60 (68.2)</td>
<td>49 (54.4)</td>
</tr>
<tr>
<td>Gout Flares</td>
<td>38 (43.7)</td>
<td>40 (45.5)</td>
<td>39 (43.3)</td>
</tr>
<tr>
<td>Infections (including viral)</td>
<td>20 (23.0)</td>
<td>16 (18.2)</td>
<td>15 (16.7)</td>
</tr>
<tr>
<td>COVID-19(^2)</td>
<td>6 (6.9)</td>
<td>5 (5.7)</td>
<td>6 (6.7)</td>
</tr>
<tr>
<td>Infusion-related AEs (24h)</td>
<td>6 (6.9)</td>
<td>6 (6.8)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>Infusion reactions (1h) incl. anaphylaxis</td>
<td>3 (3.4)</td>
<td>4 (4.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hypertriglyceridemia(^3)</td>
<td>7 (8.0)</td>
<td>8 (9.1)</td>
<td>6 (6.7)</td>
</tr>
<tr>
<td>Stomatitis(^4)</td>
<td>8 (9.2)</td>
<td>3 (3.4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Proteinuria/renal impairment/↑creatinine</td>
<td>1 (1.1)</td>
<td>2 (2.3)</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Thromboembolism</td>
<td>0 (0)</td>
<td>1 (1.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>0 (0)</td>
<td>2 (2.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Miscellaneous(^5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (2.2)</td>
</tr>
</tbody>
</table>

- No increase in gout flares between active treatment and placebo groups
- Low incidence of infusion reactions in high and low dose groups
- All IRs occurred with the first three infusions and resolved when infusions were stopped
- Stomatitis in treatment groups were all mild to moderate intensity and did not result in withdrawal of any patient

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\(1\) AESIs included in protocol as agreed with FDA; No other TEAEs ≥5%
\(2\) There were no other individual infections >2%
\(3\) Dyslipidemia/hypertriglyceridemia/hyperlipidemia
\(4\) Stomatitis/oral ulcer/aphthous ulcer; 67% mild, 33% moderate
\(5\) Influenza-like (1), ↑LDL (1)
### Serious Adverse Events (SAEs)

#### Pooled Studies at 6-Month Primary Endpoint

<table>
<thead>
<tr>
<th></th>
<th>High dose (87) n (%)</th>
<th>Low dose (88) n (%)</th>
<th>Placebo (90) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subjects with ≥1 SAE</strong></td>
<td>6 (6.9)</td>
<td>13 (14.8)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td><strong>Subjects with treatment-related SAE</strong></td>
<td>3 (3.4) (^1)</td>
<td>3 (3.4) (^2)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Primary per Patient**

<table>
<thead>
<tr>
<th>Category</th>
<th>High dose n (%)</th>
<th>Low dose n (%)</th>
<th>Placebo n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>0 (0)</td>
<td>4 (4.5) (^3)</td>
<td>1 (1.1) (^4)</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>2 (2.3)</td>
<td>2 (2.3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gout Flare</td>
<td>1 (1.1)</td>
<td>1 (1.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>GI, Renal, Liver, &amp; Neuro</td>
<td>2 (2.3) (^5)</td>
<td>4 (4.5) (^6)</td>
<td>1 (1.1) (^7)</td>
</tr>
<tr>
<td>Cardio &amp; Vascular</td>
<td>1 (1.1) (^8)</td>
<td>2 (2.3) (^9)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

1. **US:** Gout flare (1), **Global:** Anaphylaxis (2);  
2. **US:** Anaphylaxis (2), Gout Flare (1)  
3. **US:** Periodontal infection/cellulitis (1), C. diff colitis (1), **Global:** Pneumonia/Resp Failure/Sepsis (1); infected tophus (1)  
4. **Global:** COVID-19 (1)  
5. **US:** GI bleed (1) **Global:** Acute Renal Injury (1)

- Six patients (3.4%) in the pooled active treatment groups had an SAE related to treatment (n=4 anaphylaxis, n=2 gout flares)
- No other SAEs were evaluated as treatment-related

**Notes:**

- **Global:** Enteritis (1)  
- **Global:** Diverticular Hemorrhage (1)  
- **Global:** Angina Pectoris (1)  
- **Global:** Pulmonary Embolism (1) Acute myocardial infarction (1)
Conclusions

• For all treatment groups, the DISSOLVE studies **met the primary efficacy endpoint** of achieving and maintaining a sUA < 6 mg/dL for ≥80% of the time during the sixth treatment period.

• The response rate\(^1\) and sUA reduction were statistically significant against placebo with **once-monthly SEL-212**

• The high dose response rate was **56%** in DISSOLVE I and **46%** in DISSOLVE II

• **For patients ≥50 years old**, the high dose response rate was **65%** and **47%** in DISSOLVE I & II, respectively

• Infusion reaction incidence was **3.4%** in the combined **high dose** groups

• The **efficacy and safety of SEL-212** in these Phase 3 trials indicate that **targeted immunomodulation with nanoencapsulated rapamycin** may have the potential to provide a **new once-monthly uricase-based treatment option** for patients with refractory gout.

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sUA, serum uric acid

\(^1\) Defined as the % of patients who achieved and maintained a sUA < 6 mg/dL for at least 80% of the time during the sixth 28-day treatment period (TP6).
Thank you to the entire team

most importantly

participating patients & their families