Collagen Turnover Biomarkers Associate with Active Psoriatic Arthritis and Decrease with Guselkumab Treatment in a Phase 3 Clinical Trial (DISCOVER-2)

Georg Schett, PhD\textsuperscript{1}, Matthew J. Loza, PhD\textsuperscript{2}, Arumugam Palanichamy, PhD\textsuperscript{2}, Oliver FitzGerald MD\textsuperscript{3}, Christopher Ritchlin, MD, MPH\textsuperscript{4}, Anne-Christine Bay-Jensen, PhD\textsuperscript{5}; Signe Holm Nielsen, PhD\textsuperscript{5}; Sheng Gao, PhD\textsuperscript{2}, Elizabeth C. Hsia, MD, MSCE\textsuperscript{2,6}, Alexa P. Kollmeier, MD\textsuperscript{7}, Xie L. Xu, PhD\textsuperscript{7}, Frédéric Baribaud, PhD\textsuperscript{2}, Kristen Sweet, PhD\textsuperscript{2}

\textsuperscript{1}Friedrich Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany; \textsuperscript{2}Janssen Research & Development LLC, Spring House, Pennsylvania, USA; \textsuperscript{3}University College Dublin, School of Medicine, Conway Institute for Biomolecular Research, Dublin 4, Ireland; \textsuperscript{4}University of Rochester, Medical Center, Rochester, New York, USA; \textsuperscript{5}Nordic Bioscience, Herlev, Denmark; \textsuperscript{6}University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA; \textsuperscript{7}Janssen Research & Development, LLC, San Diego, California, USA

Corresponding author:

Georg Schett
Email: georg.schett@uk-erlangen.de
Supplementary Figure 1. Collagen Degradation and Formation Biomarkers in the Serum of PsA Patients Compared to Healthy Controls

Healthy controls (N=76) were demographically matched (age and sex) to PsA biomarker subset (N=260). Values are median (plus [+] marks represent mean). Boxes represent interquartile range, while whiskers represent the minimum and maximum values. adj, adjusted; PsA, psoriatic arthritis; adj p<0.05
**Supplementary Table 1. Mean Biomarker Concentrations at Baseline in the Guselkumab and Placebo Groups and Healthy Subjects**

| Patients, N | Guselkumab 100 mg Q4W | Guselkumab 100 mg Q8W | Placebo | Healthy |
|-------------|------------------------|------------------------|---------|---------|
| N           | 82                     | 92                     | 86      | 76      |
| Biomarker   | Log$_2$ (ng/mL) | SD | Log$_2$ (ng/mL) | SD | Log$_2$ (ng/mL) | SD | Log$_2$ (ng/mL) | SD |
| C1M         | 6.50 | 0.83 | 6.27 | 0.87 | 6.48 | 1.05 | 4.73 | 0.29 |
| C2M         | -1.66 | 0.67 | -1.54 | 0.64 | -1.64 | 0.56 | -1.70 | 0.52 |
| C3M         | 4.04 | 0.40 | 3.96 | 0.39 | 4.06 | 0.43 | 3.30 | 0.44 |
| C4M         | 5.43 | 0.44 | 5.36 | 0.47 | 5.40 | 0.56 | 4.83 | 0.37 |
| C6M         | 4.92 | 0.54 | 4.89 | 0.55 | 5.02 | 0.55 | 3.46 | 0.67 |
| C10C        | 11.66 | 0.28 | 11.70 | 0.33 | 11.65 | 0.37 | 11.44 | 0.39 |
| PRO-C1      | 6.52 | 0.89 | 6.66 | 0.70 | 6.54 | 0.73 | 6.36 | 0.73 |
| PRO-C2      | 4.47 | 0.53 | 4.47 | 0.46 | 4.45 | 0.55 | 4.35 | 0.77 |
| PRO-C3      | 3.58 | 0.50 | 3.60 | 0.49 | 3.45 | 0.54 | 3.03 | 0.44 |
| PRO-C4      | 12.02 | 0.59 | 12.04 | 0.42 | 12.05 | 0.37 | 11.97 | 0.31 |
| PRO-C6      | 3.24 | 0.53 | 3.29 | 0.50 | 3.18 | 0.48 | 2.77 | 0.47 |

Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation
### Supplementary Table 2. Efficacy results at Week 24 for patients in the DISCOVER-2 Biomarker Subset and the overall DISCOVER-2 study population.

| Response at Week 24 | DISCOVER-2 Biomarker Subset | DISCOVER-2 Study Cohort |
|---------------------|-----------------------------|--------------------------|
| Patients, N        | Gusekumab 100 mg Q4W        | Placebo Q8W              |
|                    | Placebo Q4W                 |
|                    | Gusekumab 100 mg Q8W        | Placebo Q8W              |
| Acro (≥20%)        | 55 (67.1%)                  | 156 (63.7%)              |
| Acro (≥50%)        | 22 (26.8%)                  | 33 (35.9%)               |
| PASI75*            | 64 (78.0%)                  | 144/184 (78.3%)          |
| PASI90*            | 49 (59.8%)                  | 112/184 (60.9%)          |

Data reported as n (%) or n/N (%).

*PASI responses were assessed in patients with ≥3% body surface area psoriatic involvement and an Investigator’s Global Assessment score of ≥2 at baseline. All patients included in the Biomarker Subset met these criteria.

ACR20/50, ≥20%/≥50% improvement in American College of Rheumatology response criteria; PASI75/90, ≥75%/≥90% improvement in Psoriasis Area and Severity Index score; Q4W, every 4 weeks; Q8W, every 8 weeks.
### Supplementary Table 3. Guselkumab Reduces Serum levels of C1M, C3M, C4M, and C6M Relative to Baseline Levels and Relative to Placebo

| Biomarkers | Q4W   | Q8W   | Guselkumab Q4W | Q4W   | Q8W   |
|------------|-------|-------|----------------|-------|-------|
| C1M        |       |       |                |       |       |
| W4 vs BL   | 0.01  | 0.15  | 0.78           | 0.34  | 0.52  |
| W24 vs BL  | <0.0001 | <0.0001 | 0.02           | W24: Guselkumab vs placebo |
| W52 vs BL  | <0.0001 | <0.0001 | <0.0001        |
| C3M        |       |       |                |       |       |
| W4 vs BL   | 0.10  | 0.24  | 0.87           | 0.49  | 0.59  |
| W24 vs BL  | <0.0001 | <0.0001 | 0.17           | W24: Guselkumab vs placebo |
| W52 vs BL  | 0.0001 | <0.0001 | <0.0001        |
| C4M        |       |       |                |       |       |
| W4 vs BL   | 0.10  | 0.15  | 0.88           | 0.34  | 0.33  |
| W24 vs BL  | <0.0001 | <0.0001 | 0.23           | W24: Guselkumab vs placebo |
| W52 vs BL  | <0.0001 | <0.0001 | <0.0001        |
### Supplementary Table 3. Guselkumab Reduces Serum levels of C1M, C3M, C4M, and C6M Relative to Baseline Levels and Relative to Placebo

| Biomarkers | Guselkumab 100 mg | Placebo → | Guselkumab 100 mg |
|------------|-------------------|-----------|-------------------|
|            | Q4W               | Q8W       | Q4W               |
| C6M        |                   |           |                   |
| W4 vs BL   | **0.02**          | 0.15      | 0.78              |
|            | W4: Guselkumab vs placebo |
| W24 vs BL  | <0.0001           | <0.0001   | **0.02**          |
|            | W24: Guselkumab vs placebo |
| W52 vs BL  | <0.0001           | <0.0001   | <0.0001           |

GUS Q4W, N=82; GUS Q8W, N=92; placebo, N=86. Adj, adjusted; BL, baseline; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week

All values were adjusted p values.

Bolded values indicate significant difference (p<0.05).