

## Supporting Information

**Supplement to article titled:** Safety, Pharmacokinetics, and Efficacy of 1.5% Ruxolitinib Gel (HDM3010) in Adult Patients with Prurigo Nodularis: A Phase I/II, Randomized, Double-Blind, Vehicle-Controlled Multicenter Clinical Trial

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**The authors have provided this Supporting Information to provide readers additional information about their work.**

**Table S1 Safety summary**

|                                             | <b>HDM3010<br/>QD (N=16)<br/>n (%)</b> | <b>Vehicle QD<br/>(N=8)<br/>n (%)</b> | <b>HDM3010<br/>BID (N=16)<br/>n (%)</b> | <b>Vehicle BID<br/>(N=9)<br/>n (%)</b> | <b>Total<br/>(N=49)<br/>n (%)</b> |
|---------------------------------------------|----------------------------------------|---------------------------------------|-----------------------------------------|----------------------------------------|-----------------------------------|
| TEAEs with at least once                    | 3 (18.8)                               | 1 (12.5)                              | 4 (25.0)                                | 5 (55.6)                               | 13 (26.5)                         |
| TEAEs by worst CTCAE severity grade         |                                        |                                       |                                         |                                        |                                   |
| Grade 1                                     | 3 (18.8)                               | 1 (12.5)                              | 3 (18.8)                                | 4 (44.4)                               | 11 (22.4)                         |
| Grade 2                                     | 0                                      | 0                                     | 0                                       | 1 (11.1)                               | 1 (2.0)                           |
| Grade 3                                     | 0                                      | 0                                     | 1 (6.3)                                 | 0                                      | 1 (2.0)                           |
| Grade 4                                     | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| Grade 5                                     | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| ≥ Grade 3 TEAEs                             | 0                                      | 0                                     | 1 (6.3)                                 | 0                                      | 1 (2.0)                           |
| Serious TEAEs                               | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| TEAEs leading to study drug discontinuation | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| TEAEs leading to study drug interruption    | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| TEAEs related to local tolerability         | 1 (6.3)                                | 0                                     | 0                                       | 0                                      | 1 (2.0)                           |
| TRAEs with at least once                    | 1 (6.3)                                | 0                                     | 1 (6.3)                                 | 0                                      | 2 (4.1)                           |
| TRAEs by worst CTCAE severity grade         |                                        |                                       |                                         |                                        |                                   |
| Grade 1                                     | 1 (6.3)                                | 0                                     | 0                                       | 0                                      | 1 (2.0)                           |
| Grade 2                                     | 0                                      | 0                                     | 1 (6.3)                                 | 0                                      | 1 (2.0)                           |
| Grade 3                                     | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| Grade 4                                     | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| Grade 5                                     | 0                                      | 0                                     | 0                                       | 0                                      | 0                                 |
| TRAEs related to local tolerability         | 1 (6.3)                                | 0                                     | 0                                       | 0                                      | 1 (2.0)                           |

Abbreviations: QD, once daily; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events (Version 5.0); TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event;

Note: Data are presented as number of patients (percentage). ≥Grade 3 TEAEs are defined as all adverse events with a CTCAE grade of 3 or higher. Serious TEAEs refer to any adverse event that meets the criteria for a serious adverse event. TRAEs refer to adverse events considered by the investigator to be related or possibly related to the investigational product. Local tolerability-related events refer to skin reactions at the application site.

**Table S2** Summary of pharmacokinetic parameters following initial dose administration (D1) in patients with prurigo nodularis

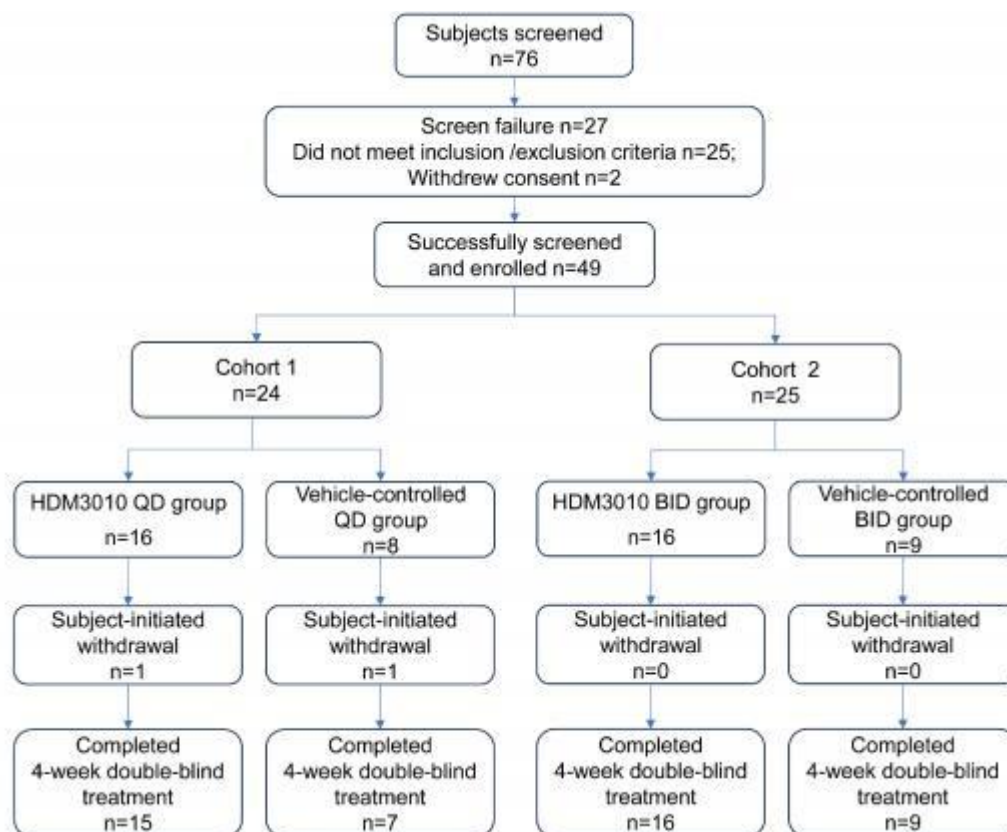
| Group                    | Visit | Statistic | Dose (mg) | C <sub>max</sub><br>(ng/mL) | AUC <sub>0-t</sub> (h.ng/mL) | T <sub>max</sub> (h) |
|--------------------------|-------|-----------|-----------|-----------------------------|------------------------------|----------------------|
| HDM3010<br>QD<br>(N=16)  | D1    | n         | 16        | 16                          | 16                           | 16                   |
|                          |       | GeoMean   | 8.66      | 0.513                       | 7.44                         | NC                   |
|                          |       | GeoCV%    | 173.5     | 268.2                       | 318.4                        | NC                   |
|                          |       | Median    | 9.53      | 0.569                       | 9.42                         | 23.2                 |
|                          |       | Min       | 1.5       | 0.097                       | 0.695                        | 2.02                 |
|                          |       | Max       | 48        | 8.62                        | 150                          | 24                   |
| HDM3010<br>BID<br>(N=16) | D1    | n         | 16        | 16                          | 16                           | 16                   |
|                          |       | GeoMean   | 15.9      | 1.14                        | 7.73                         | NC                   |
|                          |       | GeoCV%    | 130.4     | 159.2                       | 162.9                        | NC                   |
|                          |       | Median    | 12.7      | 1.28                        | 8.91                         | 9.74                 |
|                          |       | Min       | 4.35      | 0.079                       | 0.337                        | 3.87                 |
|                          |       | Max       | 129       | 5.82                        | 42.4                         | 12.1                 |

Abbreviations: C<sub>max</sub>, maximum plasma concentration; AUC<sub>0-t</sub>, area under the concentration–time curve from time 0 to the last measurable concentration; T<sub>max</sub>, time to reach C<sub>max</sub>; GeoMean, geometric mean; GeoCV%, geometric coefficient of variation; NC, not calculated; QD, once daily; BID, twice daily;

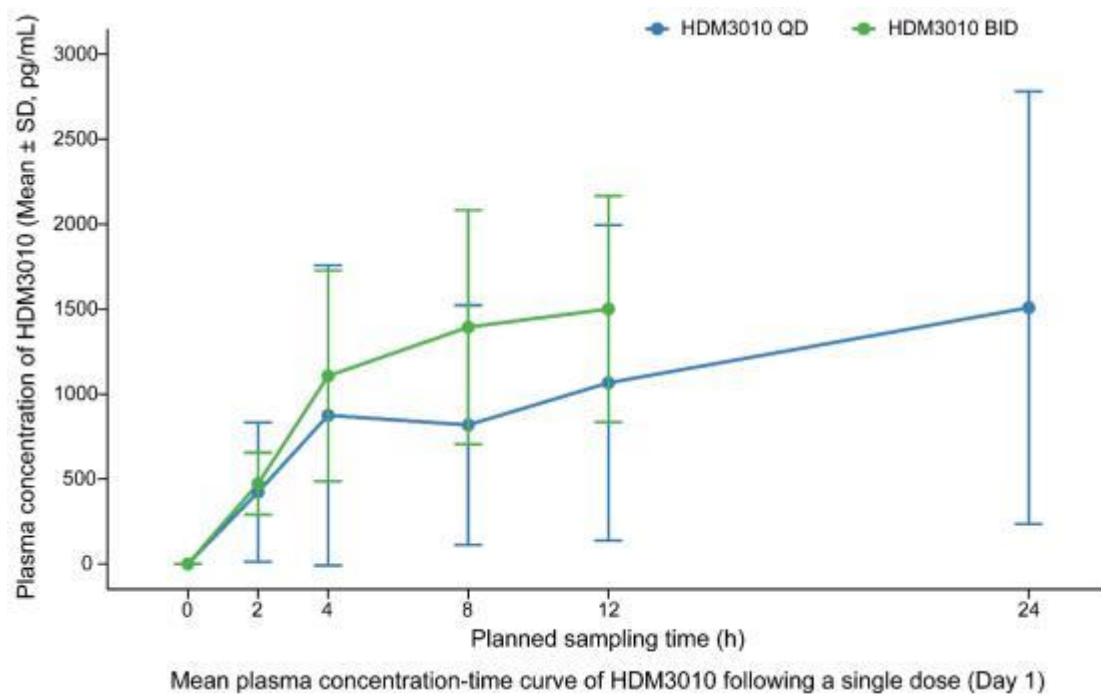
Note: Pharmacokinetic parameters were calculated based on actual dosing and sampling times. D1 refers to the first day of the double-blind treatment period. The dose shown represents the initial administered dose on D1. Tmax is presented as median (min–max). Other parameters are presented as both geometric mean (geometric CV%) and median (min–max).

**Table S3** Study sites' Ethics Committee

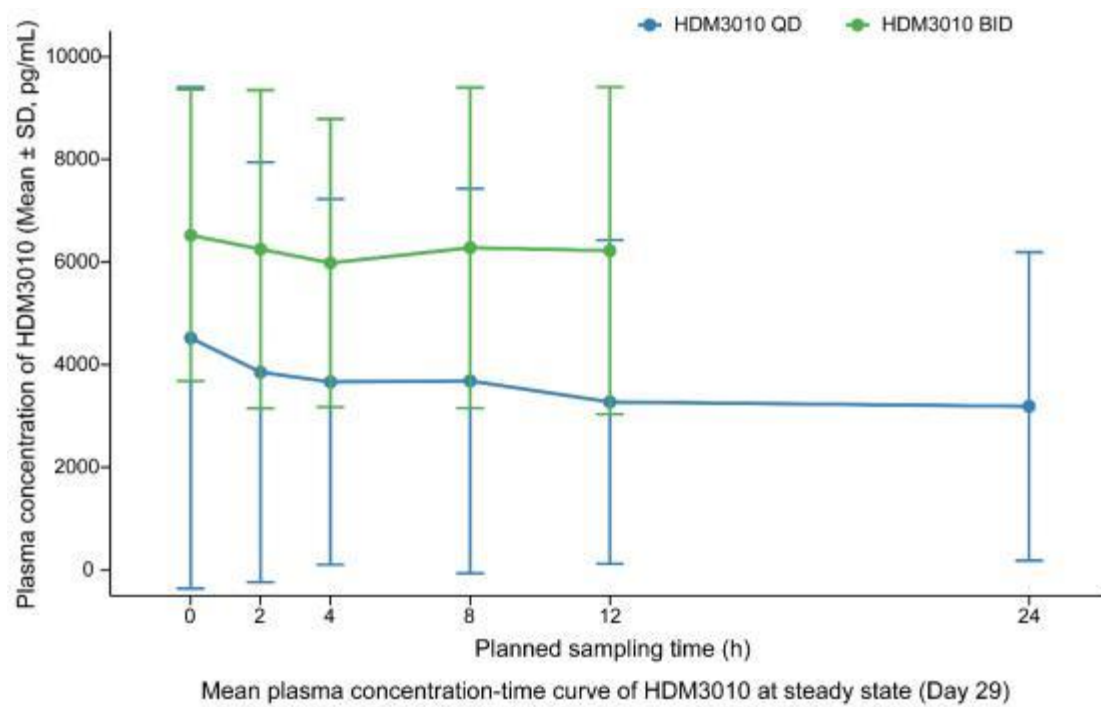
| Study site                                                                           | Ethics Committee approved number                                            |
|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Chinese Academy of Medical Sciences and Peking Union Medical College                 | KS20241626                                                                  |
| Taiyuan Central Hospital                                                             | YW2025-H202501-01                                                           |
| Dermatology Hospital, Southern Medical University                                    | YW-2025-014                                                                 |
| Xiangya Hospital, Central South University                                           | 202503045                                                                   |
| The Second Affiliated Hospital of Chongqing Medical University                       | No. 2025 Annual Review (20)                                                 |
| West China Hospital, Sichuan University                                              | No. 2025 Clinical Trial (Western Medicine) Review (42)                      |
| The Second Affiliated Hospital of Anhui Medical University                           | YW2025-058(F1)                                                              |
| The Second Affiliated Hospital of Wannan Medical College                             | LLSC2025009                                                                 |
| The First Hospital of Shanxi Medical University                                      | 2025025                                                                     |
| Chengdu Second People's Hospital                                                     | PJ2025063-1                                                                 |
| Huashan Hospital, Fudan University                                                   | (2025) Ethics Review No. (119)                                              |
| Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University | 【2025】 Medical Ethics Review No. (028)-01                                   |
| Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine                | FJ/SC.13/05.0                                                               |
| Beijing Tongren Hospital, Capital Medical University                                 | TREC2025-008                                                                |
| Zhejiang Provincial People's Hospital, People's Hospital of Hangzhou Medical College | No. Zhejiang Provincial People's Hospital Ethics Review 2025 Drug No. (016) |



**Figure S1** Patient disposition flowchart. QD, once daily; BID, twice daily

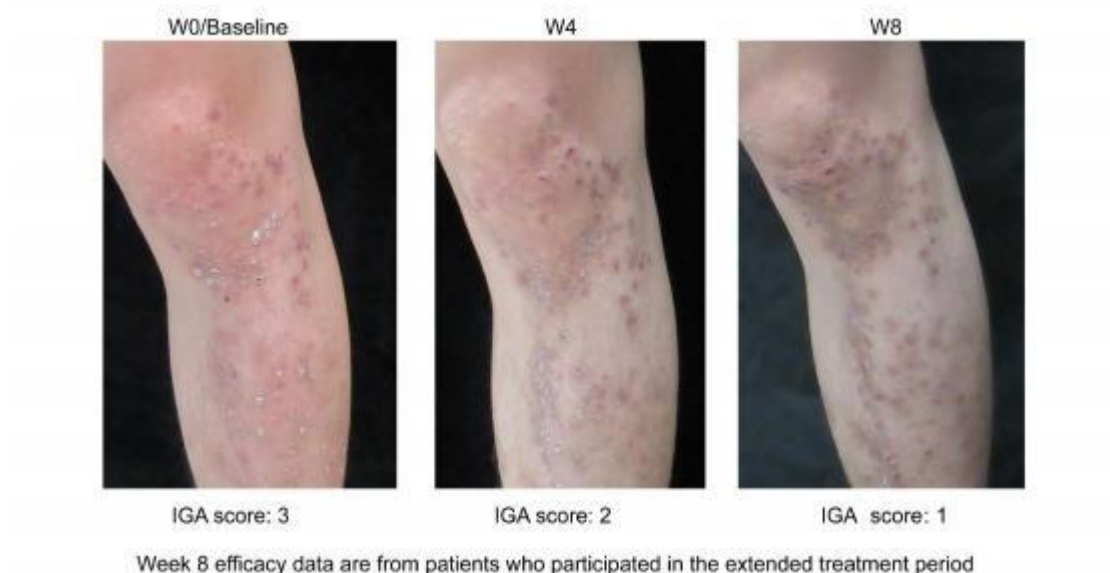


**Figure S2** Pharmacokinetics of HDM3010 on Day 1. QD, once daily; BID, twice daily



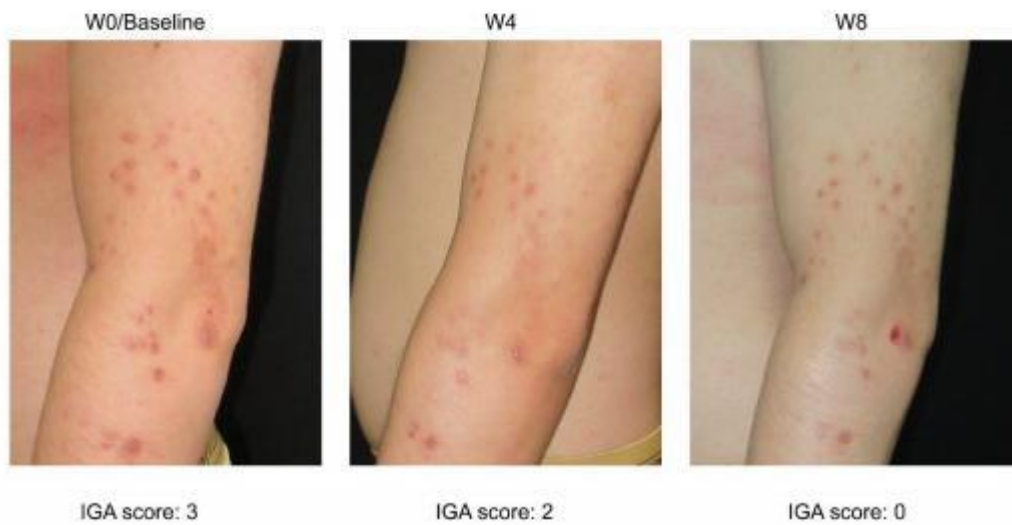
**Figure S3** Pharmacokinetics of HDM3010 on Day 29. QD, once daily; BID, twice daily

Patient 1 (left lower extremity): Change in IGA PN-S score at baseline, Week 4, and Week 8 in HDM3010 QD group



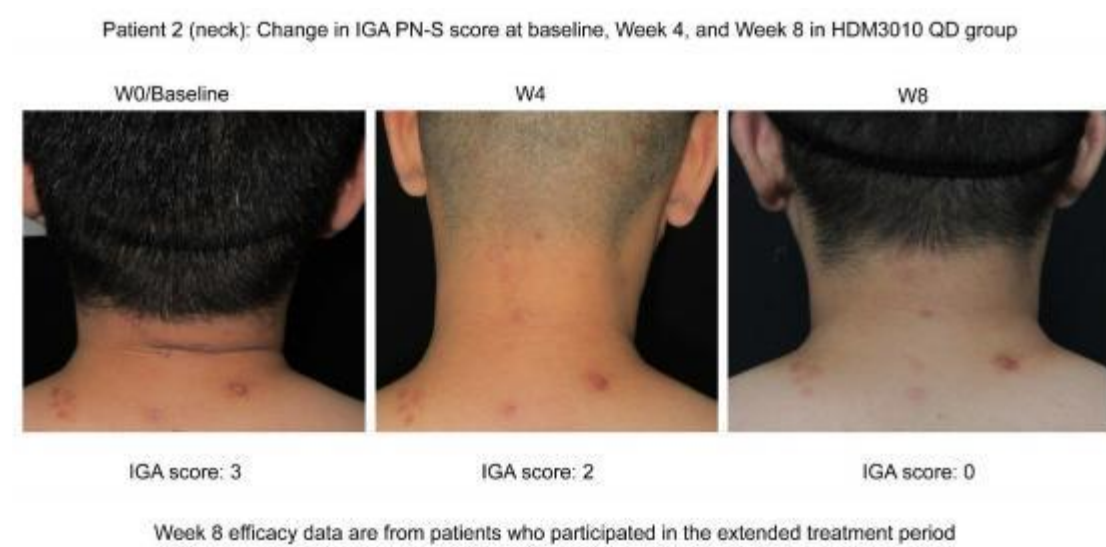
**Figure S4** Representative clinical photographs of patient 1 (left lower extremity) at baseline, Week 4, and Week 8 during treatment with HDM3010 QD. Week 8 images were obtained from the extended treatment period. IGA PN-S, Investigator's Global Assessment for Prurigo Nodularis-Stage; QD, once daily

Patient 2 (left upper extremity): Change in IGA PN-S score at baseline, Week 4, and Week 8 in HDM3010 QD group



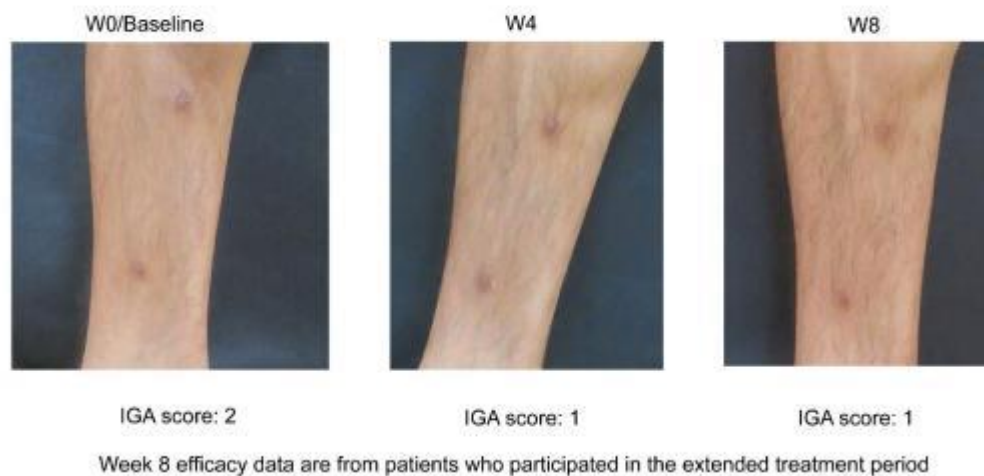
Week 8 efficacy data are from patients who participated in the extended treatment period

**Figure S5** Representative clinical photographs of patient 2 (left upper extremity) at baseline, Week 4, and Week 8 during treatment with HDM3010 QD. Week 8 images were obtained from the extended treatment period. IGA PN-S, Investigator's Global Assessment for Prurigo Nodularis-Stage; QD, once daily



**Figure S6** Representative clinical photographs of patient 2 (neck) at baseline, Week 4, and Week 8 during treatment with HDM3010 QD. Week 8 images were obtained from the extended treatment period. IGA PN-S, Investigator's Global Assessment for Prurigo Nodularis-Stage; QD, once daily

Patient 3 (right lower extremity): Change in IGA PN-S score at baseline, Week 4, and Week 8 in HDM3010 BID group



**Figure S7** Representative clinical photographs of patient 3 (right lower extremity) at baseline, Week 4, and Week 8 during treatment with HDM3010 BID. Week 8 images were obtained from the extended treatment period. IGA PN-S, Investigator's Global Assessment for Prurigo Nodularis-Stage; BID, twice daily