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Garadacimab improves quality of life in patients with hereditary angioedema: Results from the Phase 3 open-label extension study

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Disclosures

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HAE is a rare and potentially life-threatening genetic condition¹⁻³

- HAE attacks are recurrent, unpredictable, debilitating, potentially life-threatening, and substantially impair HRQoL^{1,2}
 - Attacks result from increased levels of bradykinin, a key inflammatory mediator of HAE attacks that is downstream of FXIIa in the contact activation pathway³
- Anticipation of future attacks may also cause anxiety and impact HRQoL¹
- A key goal of HAE treatment is to normalize patients' lives⁴
- There is an unmet need for:^{1,5}
 - Improved efficacy, safety, and convenience of administration
 - Novel treatments offering choices for treatment optimization

FXIIa, activated Factor XII; HAE, hereditary angioedema; HRQoL, health-related quality of life.

1. Busse P et al. *J Allergy Clin Immunol Pract* 2021;9:132-150.e3; 2. Zuraw B. *N Engl J Med* 2008;359:1027-1036; 3. Kaplan A. *Blood* 2022;139(18):2732-2733;

4. Maurer M et al. *Allergy* 2022;77:1961-1990; 5. Zanichelli A et al. *Expert Opin Emerg Drugs* 2022;27:103-110.

Garadacimab has been evaluated in a comprehensive clinical program as LTP for HAE attacks

- Garadacimab is a first-in-class, fully human mAb targeting FXIIa with completed Phase 2, pivotal Phase 3, and ongoing Phase 3 OLE studies as LTP for HAE attacks¹⁻⁴
 - Garadacimab demonstrated **durable efficacy** with a **favorable long-term safety profile**^{2,4} in:
 - Pivotal Phase 3* study: **91% reduction in HAE attacks vs run-in**
 - Pivotal Phase 3 (Month 6): **62% patients attack-free**
 - Phase 3 OLE study†: **95% reduction in HAE attacks vs run-in**
 - Phase 3 OLE†: **60% patients attack-free**
 - Substantial **QoL improvements** were observed at the earliest measurement (Day 31) and sustained to the end of the pivotal Phase 3 study⁵

QoL/PRO (by AE-QoL and TSQM II) results from a *post hoc* analysis of the ongoing Phase 3 OLE study are presented

*Primary endpoint: time-normalized number of HAE attacks per month; the mean number of HAE attacks per month was 0.27 with garadacimab vs 2.01 with placebo, P<0.0001;

†Data cut-off: Feb 13, 2023.

AE-QoL, angioedema quality of life questionnaire; FXIIa, activated Factor XII; HAE, hereditary angioedema; LTP, long-term prophylaxis; mAb, monoclonal antibody;

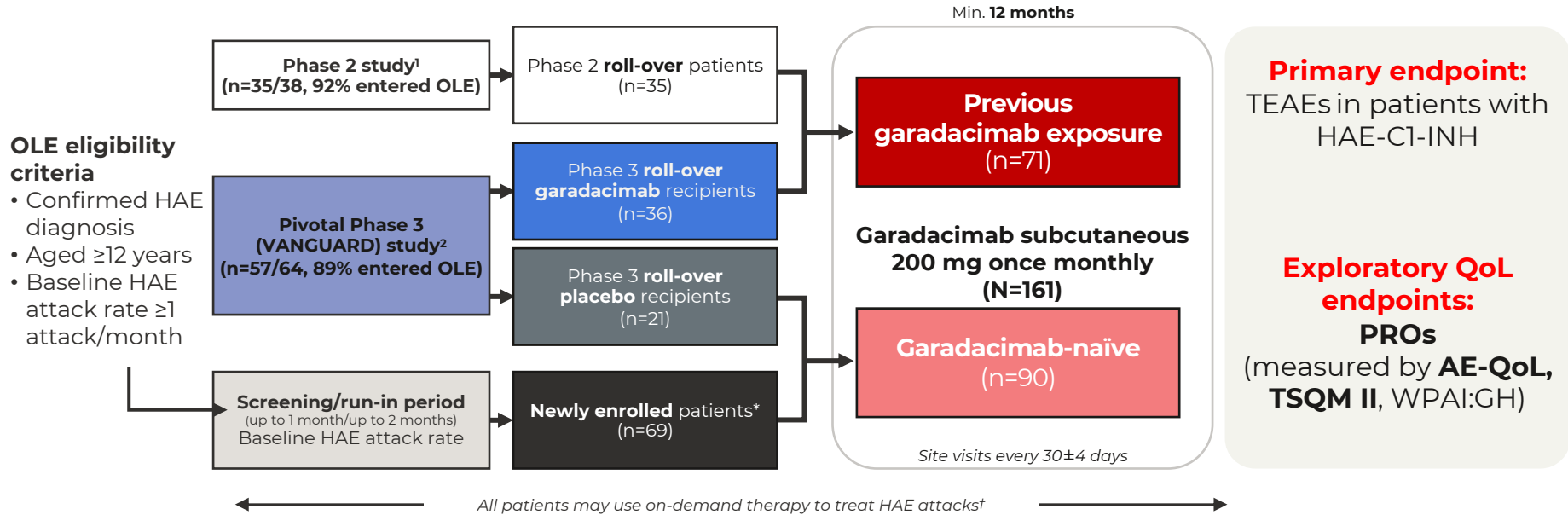
OLE, open-label extension; PRO, patient-reported outcome; QoL, quality of life; TSQM; treatment satisfaction questionnaire for medication.

1. Craig TJ et al. *Lancet* 2022;399:945–955; 2. Craig TJ et al. *Lancet* 2023;401:1079–1090; 3. ClinicalTrials.gov. NCT04739059. Available at:

<https://classic.clinicaltrials.gov/ct2/show/NCT04739059> (accessed January 2024); 4. Anderson J et al. Abstract A016. Presented at the American College for Asthma, Allergy &

Immunology Annual Scientific Meeting; Nov 9–13, 2023, Anaheim, CA, USA; 5. Staubach P et al. Abstract O923. Presented at the EAACI Congress, June 9–11, 2023, Hamburg, Germany.

QoL and PROs for garadacimab are being evaluated in a long-term Phase 3 OLE study



At data cut-off (Feb 13, 2023), 74% of patients in the Phase 3 OLE had received garadacimab for ≥ 12 months

*Newly enrolled patients received one 400 mg subcutaneous loading dose as their first dose; †Patients may use acute on-demand therapy to treat emerging episodes of edema if the medication has previously been shown to be effective.

AE-QoL, angioedema quality of life questionnaire; HAE, hereditary angioedema; HAE-C1-INH, hereditary angioedema with C1 inhibitor deficiency; OLE, open-label extension; PRO, patient-reported outcome; QoL, quality of life; TEAE, treatment-emergent adverse event; TSQM, Treatment Satisfaction Questionnaire for Medication; WPAI:GH, work productivity and activity impairment: general health.

1. Craig TJ et al. *Lancet* 2022;399:945–955; 2. Craig TJ et al. *Lancet* 2023;401:1079–1090.

QoL/PROM instruments presented today

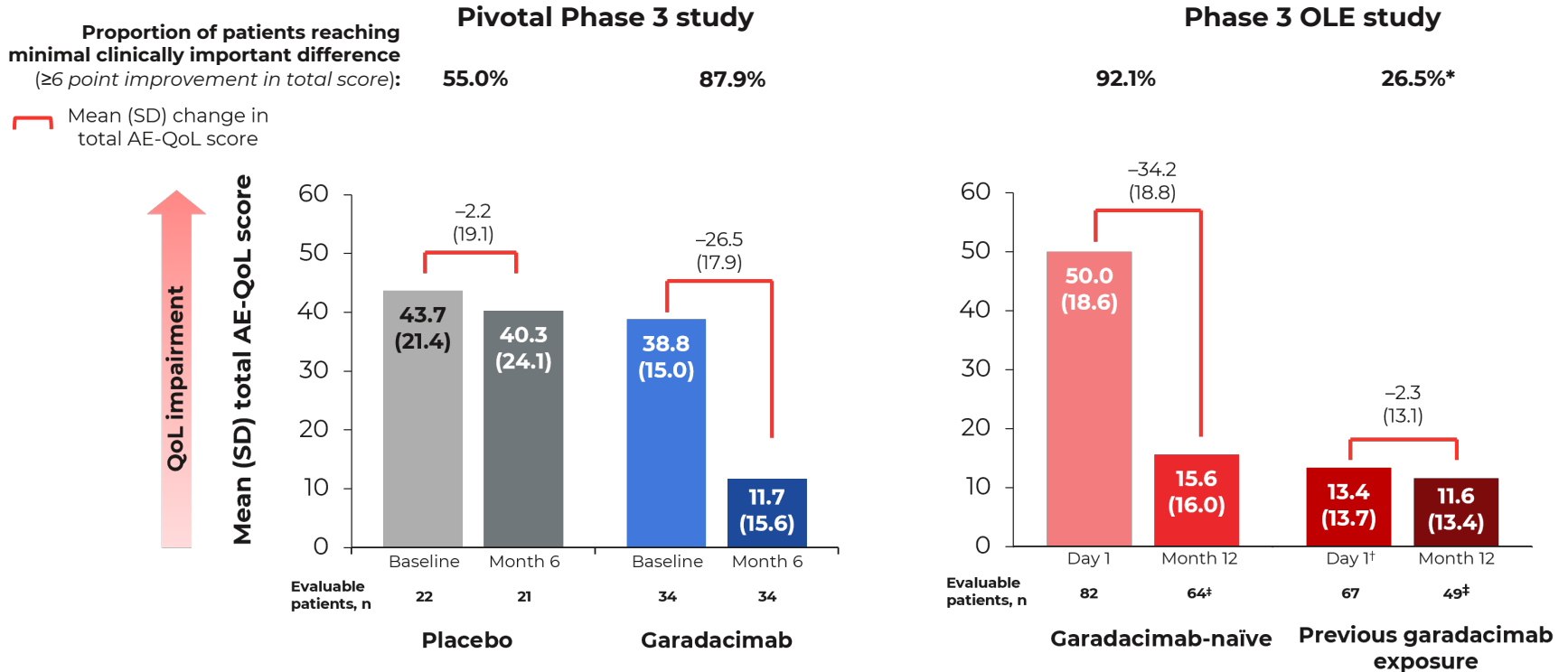
AE-QoL^{1,2}

- A validated scaled (1–5) angioedema-specific questionnaire consisting of 17 questions across four domains (functioning, fatigue/mood, fear/shame, and nutrition)
- Minimal clinically important difference – change in total score of ≥ 6 points
- Total score can be categorized by no impairment (score < 24), small impairment (24 score < 39), and moderate/large impairment (score ≥ 39)³

TSQM II⁴

- A scaled (1–5 or 1–7) and dichotomous questionnaire consisting of 11 questions across four domains (effectiveness, side effects, convenience, and global satisfaction)
- Higher scores indicate higher levels of satisfaction with treatment

Garadacimab showed long-term QoL improvement in the Phase 3 OLE study, consistent with the pivotal Phase 3 study¹



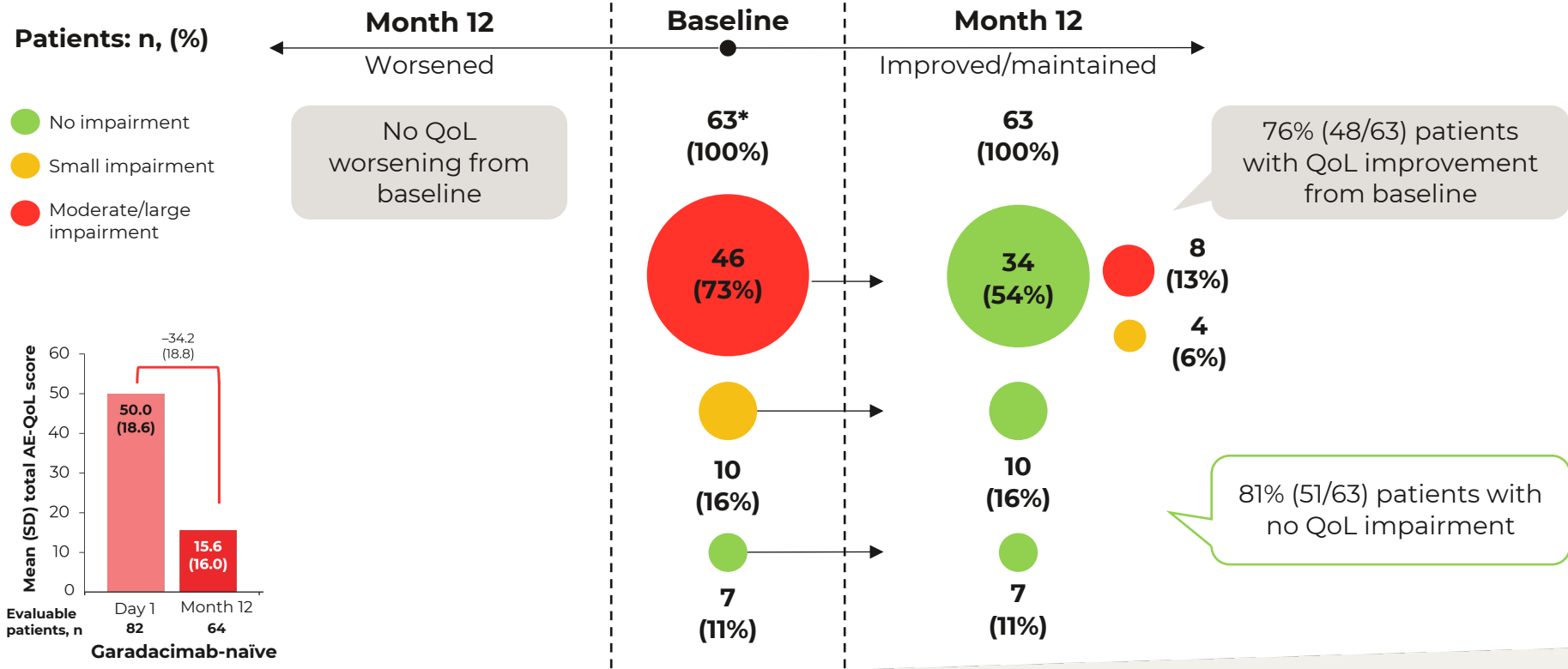
Data cut-off: Feb 13, 2023.

*Indicates improvement of ≥6 points during the OLE, 81.6% of patients experienced stable AE-QoL scores in the Phase 3 OLE after experiencing improvement in QoL in the prior study; [†]Day 1 is equivalent to last study visit date of the previously enrolled study; [‡]Decrease in evaluable patients in the OLE is due to different enrollment/roll-over times, and not due to discontinuation.

AE-QoL, angioedema quality of life questionnaire; OLE, open-label extension; QoL, quality of life; SD, standard deviation.

1. Chapdelaine H et al. *Ann Allergy Asthma Immunol* 2023;131:S15-S94.

Most garadacimab-naïve patients in the Phase 3 OLE experienced AE-QoL improvement from baseline



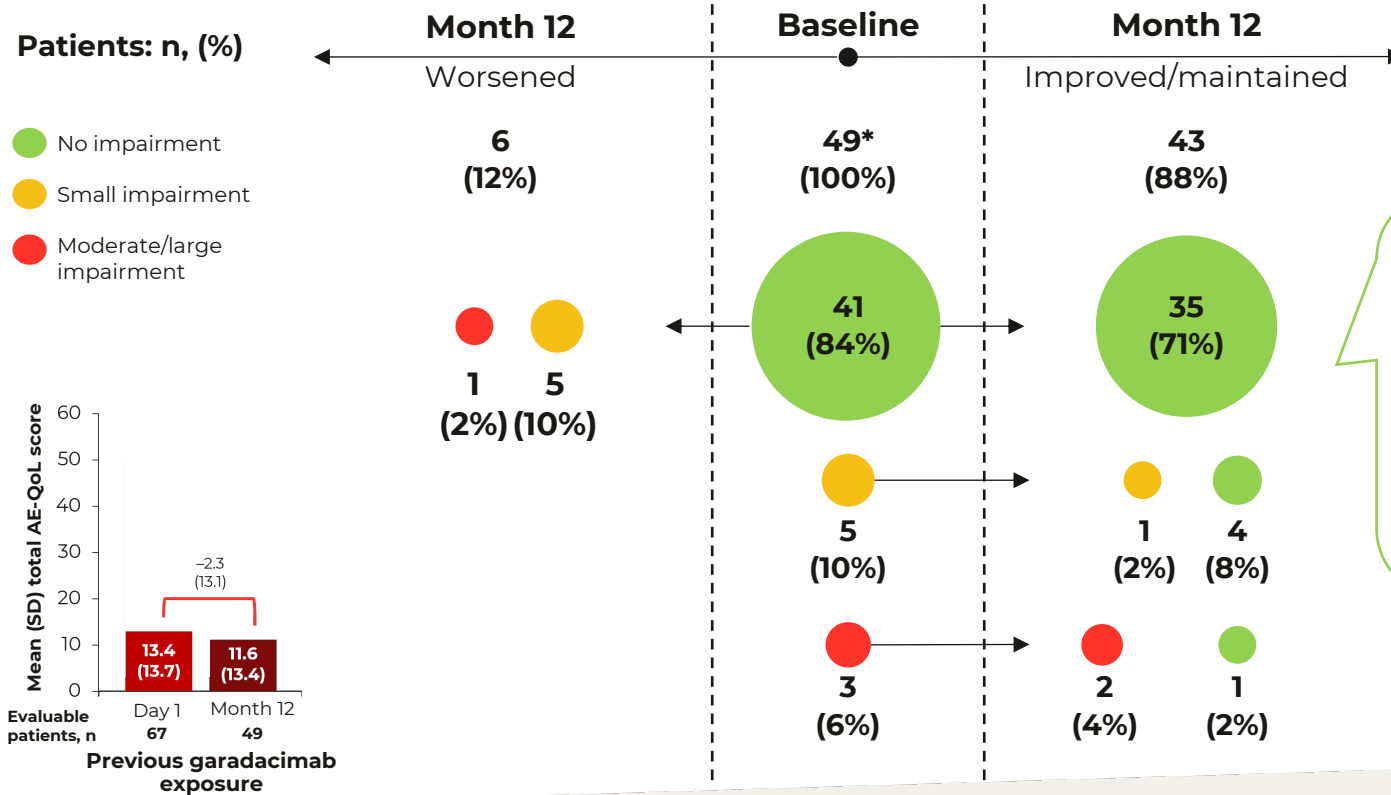
Interpretation of global AE-QoL score shifts: score <24, no impairment; 24 ≤ score <39, small impairment; score ≥39, moderate/large impairment.¹

*Total number of patients included in this *post hoc* analysis.

AE-QoL, angioedema quality of life; OLE, open-label extension; QoL, quality of life; SD, standard deviation.

1. Kulthanan K et al. *Health Qual Life Outcomes* 2019;17:160.

Most patients with previous garadacimab exposure maintained AE-QoL improvement from baseline in the Phase 3 OLE



82% (40/49) patients with no QoL impairment:

- 71% (35/49) patients maintained no QoL impairment
- 10% (4/5 and 1/3) patients with further QoL improvement

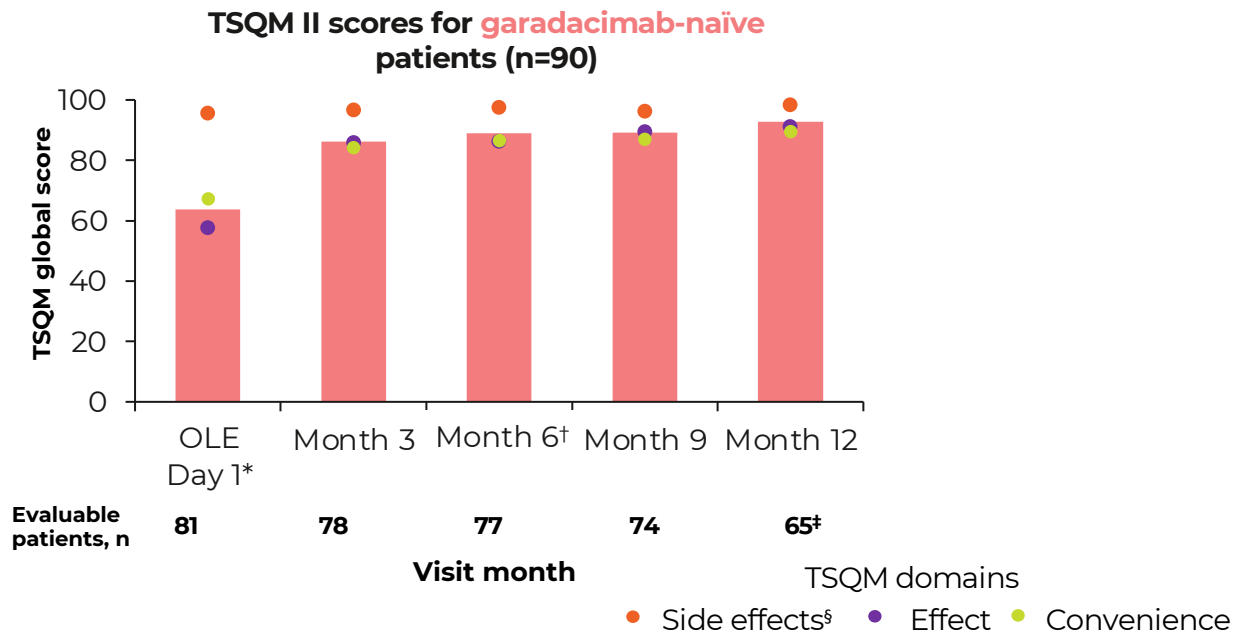
Interpretation of global AE-QoL score shifts: score <24, no impairment; 24 ≤ score <39, small impairment; score ≥39, moderate/large impairment¹

*Total number of patients included in this *post hoc* analysis.

AE-QoL, angioedema quality of life; OLE, open-label extension; QoL, quality of life; SD, standard deviation.

1. Kulthanan K et al. *Health Qual Life Outcomes* 2019;17:160.

Sustained AE-QoL improvement with garadacimab is bolstered by high treatment satisfaction in the Phase 3 OLE



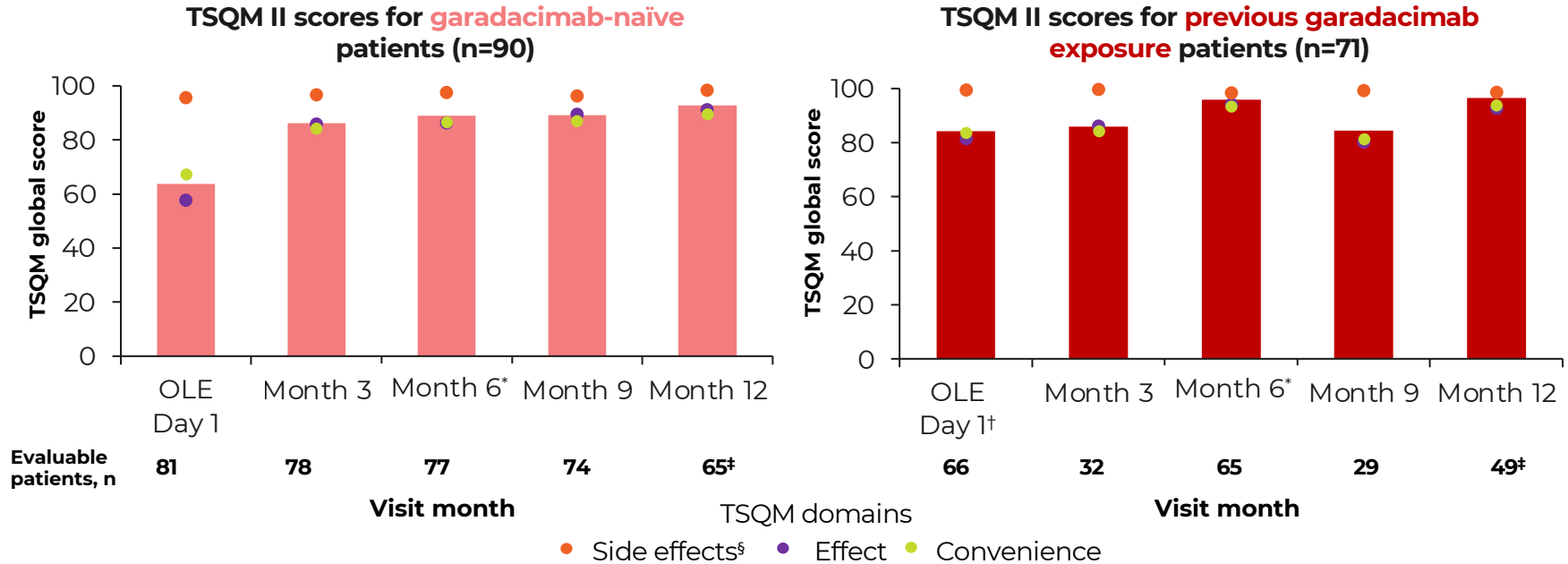
Data cut-off: Feb 13, 2023.

*Day 1 measurements in garadacimab-naïve patients refers to satisfaction with current on-demand treatment; [†]The effect and convenience domains are overlapping for Month 6;

[‡]Decrease in evaluable patient numbers in the OLE is due to different enrollment/roll-over times, and not due to discontinuation; [§]The “side effects” category is a measure of patient-reported impact of potentially experienced side effects on treatment satisfaction, and is not a safety measure.

AE-QoL, angioedema quality of life; OLE, open-label extension; TSQM II, treatment satisfaction questionnaire for medication.

Sustained AE-QoL improvement with garadacimab is bolstered by high treatment satisfaction in the Phase 3 OLE



Data cut-off: Feb 13, 2023.

*The effect and convenience domains are overlapping for Month 6; [†]Day 1 is equivalent to the last measurement from their previous study; [‡]Decrease in evaluable patient numbers in the OLE is due to different enrollment/roll-over times, and not due to discontinuation; [§]The "side effects" category is a measure of patient-reported impact of potentially experienced side effects on treatment satisfaction and is not a safety measure.

AE-QoL, angioedema quality of life; OLE, open-label extension; TSQM II, treatment satisfaction questionnaire for medication.

Garadacimab 200 mg SC once-monthly showed sustained QoL improvement and high treatment satisfaction in the Phase 3 OLE

Clinically meaningful QoL improvements consistent with reported efficacy data^{1,2}

- Pivotal Phase 3: AE-QoL mean total score improvement of 26.5 points with garadacimab vs 2.2 with placebo¹
- Phase 3 OLE:
 - Garadacimab-naïve: all patients experienced improvement from baseline and 81% reported no QoL impairment by Month 12
 - Previous garadacimab exposure: 82% of patients with maintained QoL improvement or further improvement

High treatment satisfaction, sustained long-term in the Phase 3 OLE

- >80% TSQM II scores for both garadacimab-naïve and previous garadacimab exposure patients

AE-QoL, angioedema quality of life questionnaire; MCID, minimal clinically important difference; OLE, open-label extension; PRO, patient reported outcome; QoL, quality of life; TSQM, treatment satisfaction questionnaire for medication.

1. Craig TJ et al. *Lancet* 2023;401:1079–1090; 2. Anderson J et al. *Ann. Allergy Asthma Immunol.* 2023;131:S3–S13 (Abstract A016), Presented at American College for Asthma, Allergy & Immunology Annual Scientific Meeting; Nov 9–13, 2023; Anaheim, CA, USA.