Week 12 Data from a Phase 1/2 Proof-of-Concept Study of Subcutaneous Lonigutamab (Anti–IGF-1R) in Patients with Thyroid Eye Disease (TED)

Jwu Jin Khong[1], David A Kostick[2], Jane Spadaro[3], Dinesh Selva[4], Jean-Louis deSousa[5], Krishna Tumuluri[6], Anita Grover[7], Petrus R de Jong[7,*], So Jung Imm[7], Roberta Vespignani[7,*], Shephard Mpofu[7,*], Shoaib Ugradar[8]

[1]Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, Melbourne, VIC, Australia, and Department of Surgery, University of Melbourne, Melbourne, VIC, Australia; [2]Florida Eye Specialists, Jacksonville, FL, USA; [3]Department of Ophthalmology, Corewell Health William Beaumont University Hospital, Royal Oak, MI, USA, and Kahana Oculoplastic and Orbital Surgery, Livonia, MI, USA; [4]Adelaide University, Adelaide, SA, Australia; [5]Lions Eye Institute, Nedlands, WA, Australia; [6]Westmead Hospital, Westmead, NSW, Australia, Macquarie University, Sydney, NSW, Australia, and Save Sight Institute, University of Sydney, Sydney, NSW, Australia; [7]ACELYRIN, INC., a wholly owned subsidiary of Alumis Inc., South San Francisco, CA, USA; [8]Private Practice, Beverly Hills, CA, USA. *At the time of the study.

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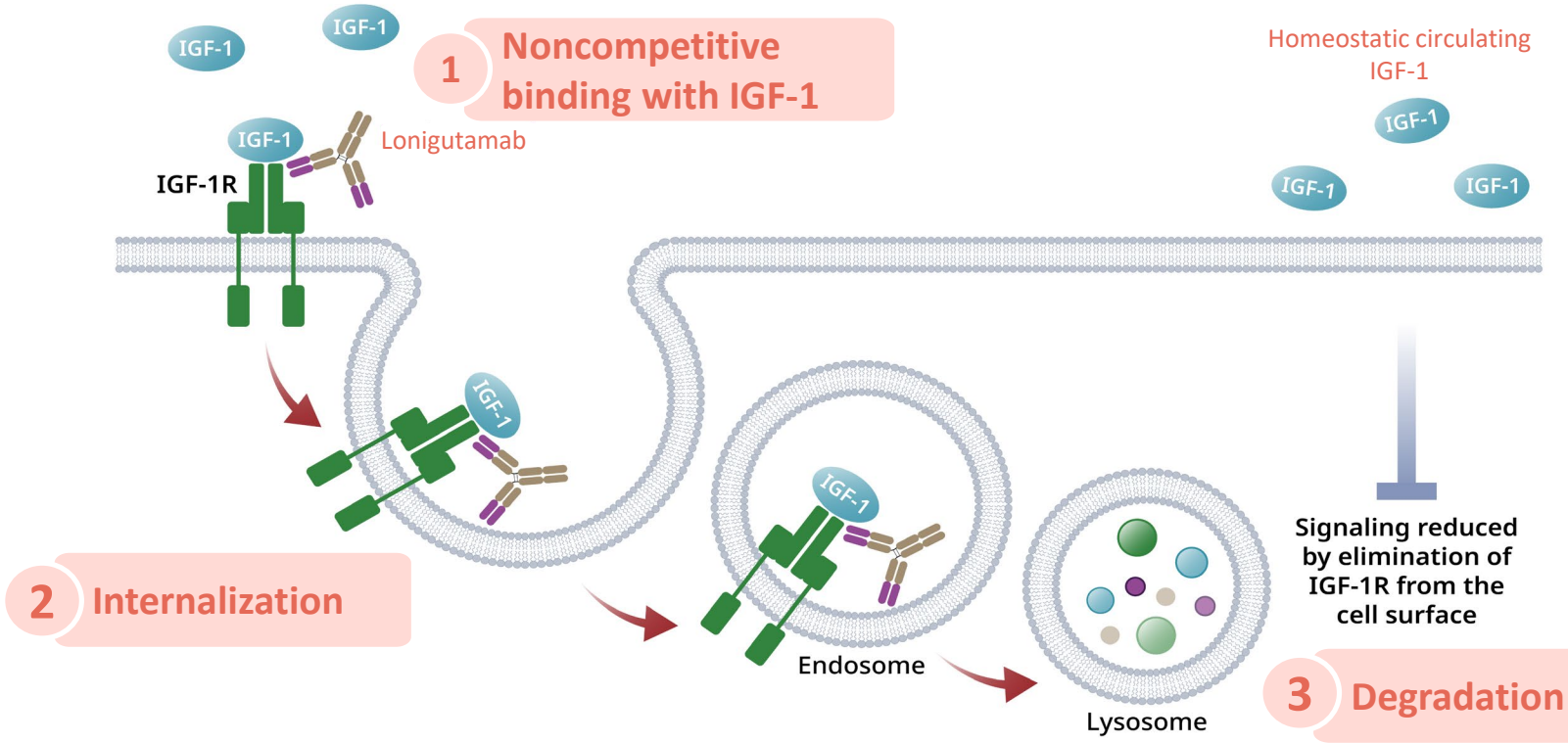
Lonigutamab[a] Mechanism of Action

〉 **Lonigutamab** is a novel, high-affinity, subcutaneously administered, **anti–IGF-1R monoclonal antibody** with a unique **noncompetitive** mechanism of action[1,2]



Potential therapeutic benefits of lonigutamab

- Convenient subcutaneous administration
- Unique noncompetitive MoA
- Potentially improved benefit-risk profile

OBJECTIVE: To present week 12 data from 3 fully enrolled cohorts of a phase 1/2 dose-ranging study evaluating lonigutamab in patients with TED (NCT05683496)[3]

Figure created with BioRender.com. [a]Lonigutamab is an investigational therapy that is not approved by any regulatory authority.
IGF-1, insulin-like growth factor 1; IGF-1R, IGF-1 receptor; MoA, mechanism of action; TED, thyroid eye disease.
1. Akla B, et al. *Mol Cancer Ther*. 2020;19(1):168-77. 2. Data on file. ACELYRIN, INC., a wholly owned subsidiary of Alumis Inc. 3. ClinicalTrials.gov identifier: NCT05683496. Updated July 1, 2025. Accessed October 7, 2025. https://clinicaltrials.gov/study/NCT05683496.

Lonigutamab Phase 1/2 Study Design

NCT05683496[1]

Key eligibility criteria

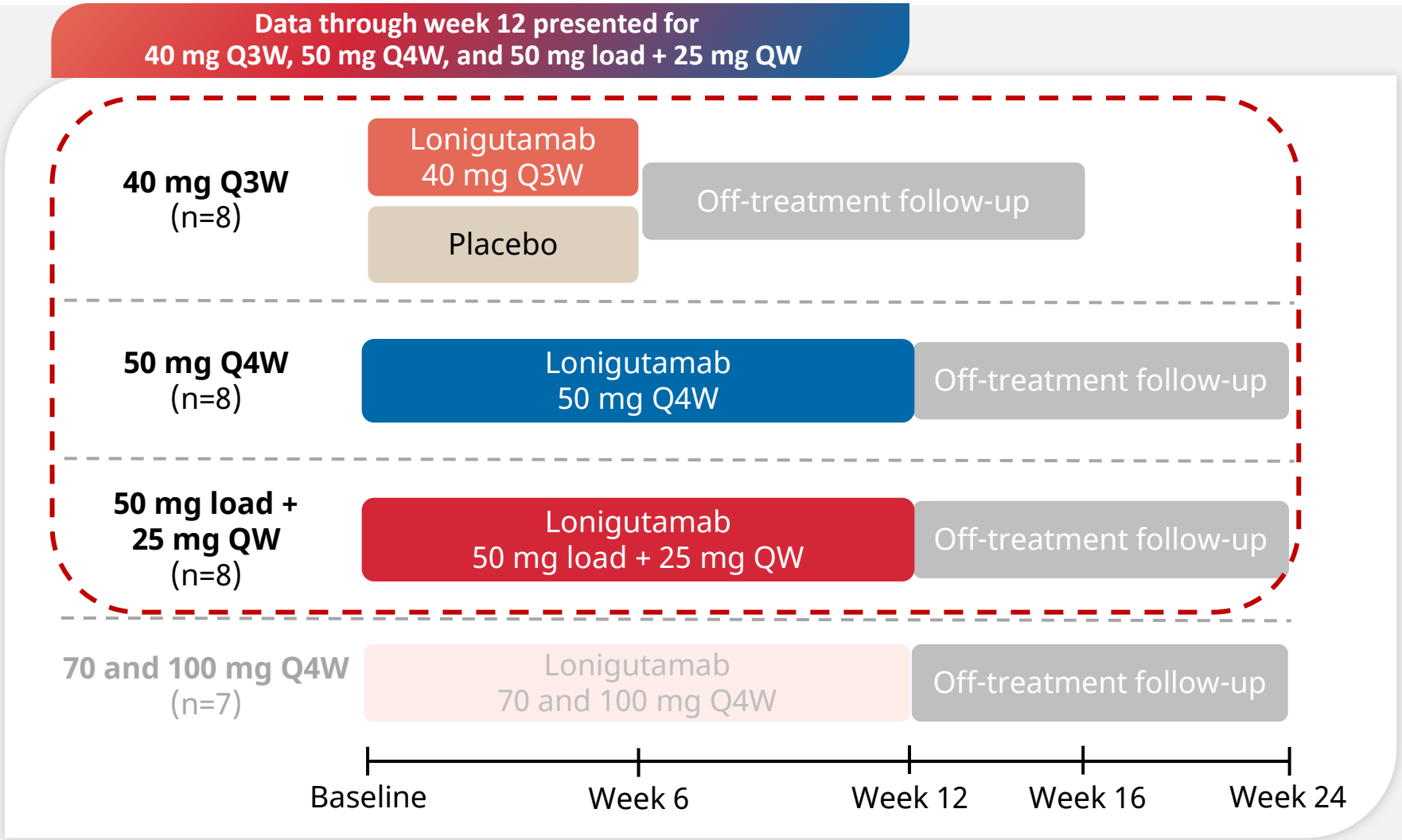
- Proptosis ≥3 mm above normal range in the study eye
- CAS ≥4 (using a 7-item scale) for the most severely affected eye
- Onset of active TED symptoms within 24 months before baseline/day 1

Efficacy endpoints

- Proptosis response (≥2-mm reduction in the study eye)
- CAS (≥2-point improvement; score of 0/1)
- Diplopia response (improvement in ≥1 Bahn-Gorman grade)
- GO-QoL (change from baseline)

Safety endpoints

- Incidence and characterization of nonserious and serious TEAEs



40 mg Q3W data as of December 6, 2023; 50 mg Q4W and 50 mg load + 25 mg QW data as of December 12, 2024.

CAS, Clinical Activity Score; GO-QoL, Graves' Ophthalmopathy Quality of Life; QW, every week; Q3W, every 3 weeks; Q4W, every 4 weeks; TEAE, treatment-emergent adverse event; TED, thyroid eye disease.

1. ClinicalTrials.gov identifier: NCT05683496. Updated July 1, 2025. Accessed October 7, 2025. https://clinicaltrials.gov/study/NCT05683496.

Summary of Efficacy at Week 12 in Lonigutamab-Treated Patients

First and Only Anti–IGF-1R to Demonstrate Efficacy in TED via Subcutaneous Route of Administration

Lonigutamab 40 mg Q3W[a] (n=6)		Lonigutamab 50 mg Q4W (n=8)		Lonigutamab 50 mg load + 25 mg QW (n=8)	
Proptosis	**CAS**	**Proptosis**	**CAS**	**Proptosis**	**CAS**
50% response ≥2 mm	**100%** ≥2-point improvement	**25%** response ≥2 mm	**63%** ≥2-point improvement	**63%** response ≥2 mm	**100%** ≥2-point improvement
−1.5 mm mean change	**67%** CAS 0/1 response	**−1.4 mm** mean change	**50%** CAS 0/1 response	**−1.9 mm** mean change	**38%** CAS 0/1 response
Diplopia[b]	**GO-QoL**	**Diplopia[b]**	**GO-QoL**	**Diplopia[b]**	**GO-QoL**
25% response ≥1 Bahn-Gorman improvement	**12.3** points mean change overall	**60%** response ≥1 Bahn-Gorman improvement	**14.4** points mean change overall	**50%** response ≥1 Bahn-Gorman improvement	**27.7** points mean change overall

[a]Off-treatment follow-up. No placebo-treated patients achieved proptosis response, CAS ≥2-point improvement, or diplopia response. [b]In patients with baseline diplopia >0 (40 mg Q3W, n=4; 50 mg Q4W, n=5; 50 mg load + 25 mg QW, n=6).

CAS, Clinical Activity Score; CAS 0/1, CAS of 0 or 1; GO-QoL, Graves' Ophthalmopathy Quality of Life; IGF-1R, insulin-like growth factor 1 receptor; QW, every week; Q3W, every 3 weeks; Q4W, every 4 weeks; TED, thyroid eye disease.

Lonigutamab Was Well Tolerated with No Serious Adverse Events

- All events were mild or moderate in severity, with **no grade ≥3 or serious TEAEs**
- Injection-site reactions (erythema, swelling, pain) in 7 patients were all mild
- Four patients receiving lonigutamab had AESIs
  - Tinnitus (all mild)
  - **No audiology changes or hyperglycemia or IBD events**
- One patient receiving placebo discontinued due to dysthyroid optic neuropathy

n (%)	Placebo n=2	Lonigutamab (40 mg Q3W) n=6	Lonigutamab (50 mg Q4W) n=8	Lonigutamab (50 mg load + 25 mg QW) n=8
Any TEAEs	2 (100.0)	4 (66.7)	6 (75.0)	8 (100.0)
Serious	0	0	0	0
Grade 2	0	1 (16.7)	0	3 (37.5)
Any treatment-related TEAEs	0	3 (50.0)	3 (37.5)	6 (75.0)
Any AESIs	0	3 (50.0)	1 (12.5)	0
Tinnitus	0	3 (50.0)	1 (12.5)	0
IBD	0	0	0	0
Hyperglycemia	0	0	0	0
TEAEs leading to study drug discontinuation	1 (50.0)	0	0	0
Dysthyroid optic neuropathy	1 (50.0)	0	0	0

CONCLUSION: Lonigutamab, a high-affinity, next-generation, subcutaneously administered anti–IGF-1R monoclonal antibody with a noncompetitive binding mechanism, was well tolerated and demonstrated proof of concept for clinical efficacy in patients with TED

The table reports the number and percentage of patients who experienced TEAEs through week 12.
AESI, adverse event of special interest; IBD, inflammatory bowel disease; IGF-1R, insulin-like growth factor 1 receptor; QW, every week; Q3W, every 3 weeks; Q4W, every 4 weeks; TEAE, treatment-emergent adverse event; TED, thyroid eye disease.