ACELYRIN

Lonigutamab

Thyroid Eye Disease

Phase 1/2 Proof of Concept

March 20, 2024

Forward Looking Statements and Disclaimer

This presentation contains statements that are not of historical facts, considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements include, but are not limited to, statements about the therapeutic potential of our product candidate lonigutamab, including with respect to the potential for its composition and subcutaneous administration to provide for sustained and/or improved treatment over time; the potential for its administration and composition to provide for a longer-term treatment duration versus other treatment options; the long-term safety profile of lonigutamab; the timing and commencement of a Phase 2b/3 trial and such trial's design to be a potential registrational trial; the potential market size and size of the potential patient populations for the thyroid eye disease (TED) indication we are pursuing, and other statements not of historical fact.

These forward-looking statements are based on ACELYRIN's current plans, objectives and projections, and are inherently subject to risks and uncertainties that may cause our actual results to differ materially and adversely from those anticipated in such forward-looking statements. Such risks and uncertainties include, without limitation, those associated with the successful completion of development and regulatory activities with respect to our product candidate lonigutamab; the timing of commencement and results of our clinical trials, including the potential that future results could differ adversely from prior results such as the cohort 1 data and n=6 open-label cohort 2 data from our Phase 1/2 trial in TED presented herein; our ability to timely secure adequate supply of our product candidates; sufficient funding; legal proceedings and the outcome thereof; competitive risks; market volatility; macroeconomic conditions and other risks and uncertainties affecting ACELYRIN including those described from time to time under the heading "Risk Factors" and elsewhere in our current and future periodic and other reports filed with the Securities and Exchange Commission ("SEC"), including our most recent Quarterly Report on Form 10-Q for the quarter ended September 30, 2023. These filings are available on the SEC's website www.sec.gov. In addition, new risks may occur at any time, and we anticipate that subsequent developments could cause our views to change. Forward-looking statements herein are made of the date of this presentation, and ACELYRIN undertakes no duty to update them in the event of new information, future developments, or otherwise, except as required under applicable law. Any reader of this presentation is cautioned not to place undue reliance on these forward-looking statements.

Lonigutamab is currently under clinical investigation, and no representation is made as of the safety or efficacy of our product candidates.

In addition to our own internal research, this presentation contains information related to or based on studies and other data obtained from third-party sources. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness thereof. In addition, market data (e.g., market size) involves a number of projections, assumptions and estimates of our future performance and future performance of the markets in which we operate. There can be no guarantee of the accuracy or reliability thereof, as they are necessarily subject to a high degree of uncertainty and risk.

The information in this presentation is as of the date of this presentation, and is subject to change without notice.

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Creating an Industry Leading Immunology Company

- **Team of veteran biopharma executives** who together bring exceptional track records of developing some of the most successful medicines within immunology and beyond

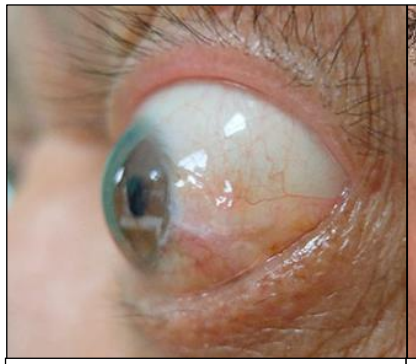
- **Building a portfolio of potential new medicines that we think have the opportunity to provide clinically meaningfully differentiated benefit to patients**
  - **We seek "diamonds in the rough"** where, based on molecule characteristics, our collective experience and expertise, and the evolving scientific and medical understanding, we can test hypotheses around clinical differentiation for patients

- **Robust pipeline of clinical programs** across several indications representing multi-billion-dollar opportunities in the aggregate
  - **Izokibep is a "pipeline-in-a-program"** in late-stage development for multiple immunological indications including psoriatic arthritis (PsA), hidradenitis suppurativa (HS), axial spondyloarthritis (AxSpA) and uveitis
  - **Lonigutamab has demonstrated proof-of-concept** as a subcutaneously delivered therapy for thyroid eye disease (TED) with the goal to improve upon efficacy, safety as well as convenience for patients
  - **SLRN-517 is an early program** targeting mast cell-driven diseases

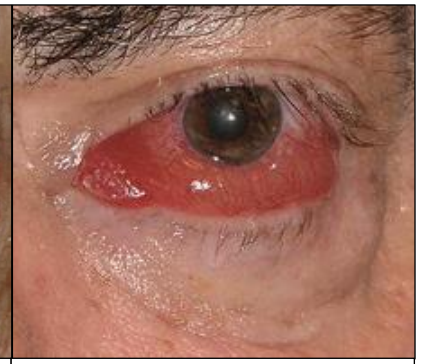
- **Well-capitalized** having secured more than $1 billion in private and public capital since founding in 2020

Thyroid Eye Disease is a Vision-Threatening Autoimmune Disease

Unmet Efficacy and Safety Needs Persist for TED Patients



Proptosis



Redness

Diplopia

TED is a debilitating disease with many life-impacting manifestations

- Characterized by progressive inflammation that can lead to **irreversible damage to tissues around the eye**, threatening vision
- Impacts >100,000 patients in the U.S.

Available treatment options are suboptimal

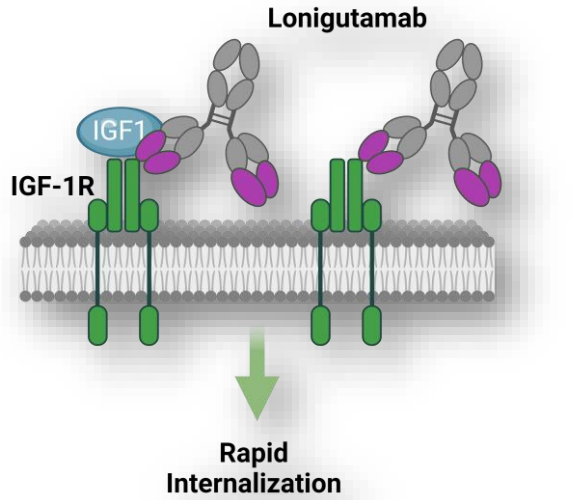
- Steroids (variable efficacy with long term safety limitations)
- IV anti-IGF-1R (short-term fixed treatment course limits depth and durability of response, safety limitations, and high patient burden)
- Surgery (complex and not curative)

Leading to important opportunities for patient impact

- **Durability of response:** TED is a chronic inflammatory condition requiring long-term treatment that could be enabled by at-home subcutaneous administration
- **Depth of response:** Opportunity for profound treatment benefit with an optimized dosing regimen, providing disease modification holistically across signs and symptoms of TED
- **Optimization of benefit-risk:** Recent safety updates to SoC label highlight hearing impairment as serious, potentially permanent effect

Lonigutamab Uniquely Impacts the IGF-1R Axis

Provides Opportunity to Optimize Benefit-Risk



High binding potency
Lonigutamab binds IGF-1R with high affinity (30 pM)[1]

Unique binding epitope
In contrast to other anti-IGF-1Rs, which compete for IGF-1 binding site, lonigutamab binds peripheral to the IGF-1 binding site

Efficient receptor internalization within minutes[1]

Depth and Durability of Clinical Response

- Current treatment response is limited by short-term, fixed, IV dosing
- SC enables long-term treatment - we hypothesize could allow for prolonged and deep clinical benefit

Optimization of Benefit-Risk

- IGF-1 in the inner ear supports regeneration following injury
- SC administration may minimize blood-labyrinth barrier penetration to the inner ear by reducing C_{max} compared to IV

Maximization of Patient Convenience

Patient-delivered, at-home, via pre-filled syringe or autoinjector offers a more convenient option to IV therapy

1 Akla 2020

Positive Phase 1/2 Proof-of-Concept Data for Lonigutamab

First Subcutaneous Anti-IGF-1R to Report Clinical Data in Thyroid Eye Disease[1]

Positive Proof of Concept for Lonigutamab

- Rapid and meaningful clinical responses for Proptosis, Clinical Activity Score, and Diplopia versus placebo
- Responses observed within 3 weeks after first subcutaneous dose and were maintained through 12 weeks; six weeks after last dose
- Well-tolerated safety profile

Potential for Differentiated Profile

- High potency anti-IGF-1R with unique impact on the IGF-1R Axis enabling the potential to optimize benefit-risk towards more complete resolution of disease
- Clinically meaningful responses achieved at lower exposures relative to standard of care:
  - Maximizing clinical benefit by enabling greater depth and durability of response with longer term treatment beyond the fixed regimen of standard of care
  - Minimizing safety liability by reducing C_{max} compared to IV therapy and penetration to the inner ear which may drive hearing impairment

Next Steps

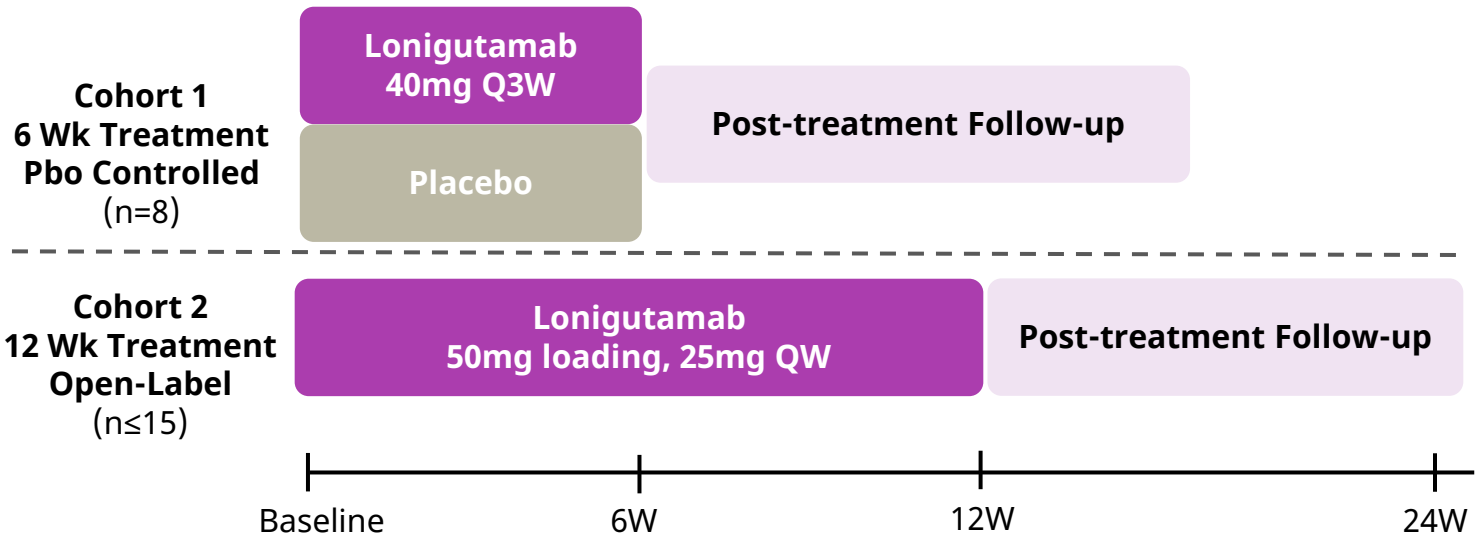
- Proof of concept achieved with placebo-controlled Cohort 1; supports monthly dosing and the potential to optimize clinical benefit-risk for patients
- Cohort 2 data further validates POC and enables continued refinement of dose level and regimen
- Phase 2b/3 trial in Thyroid Eye Disease planned to be initiated in the second half of 2024; designed to be the first of 2 registrational studies

1 Based on publicly reported data [in the U.S. and EU].

Phase 1/2 Evaluating Lonigutamab in TED

Screening/ Eligibility

- Proptosis defined in the study eye as ≥3 mm above normal
- Clinical Activity Score (CAS) ≥4 (using a 7-item scale) for the most severely affected eye
- Onset of active TED symptoms within 15 months prior to the baseline



Efficacy Endpoints

- Proptosis (reduction in eye bulging)
- Clinical Activity Score (change in CAS)
- Diplopia (reduction in double vision)

Safety

- Incidence and characterization of nonserious and serious treatment emergent adverse events (TEAEs)

Proptosis measured by hertel exophthalmometer
Cohort 3 evaluating monthly dosing ongoing
Two Dose Healthy Subject PK study completed; data not included in this presentation

Cohort 1: 40mg Q3W

Placebo-Controlled (n = 6:2)

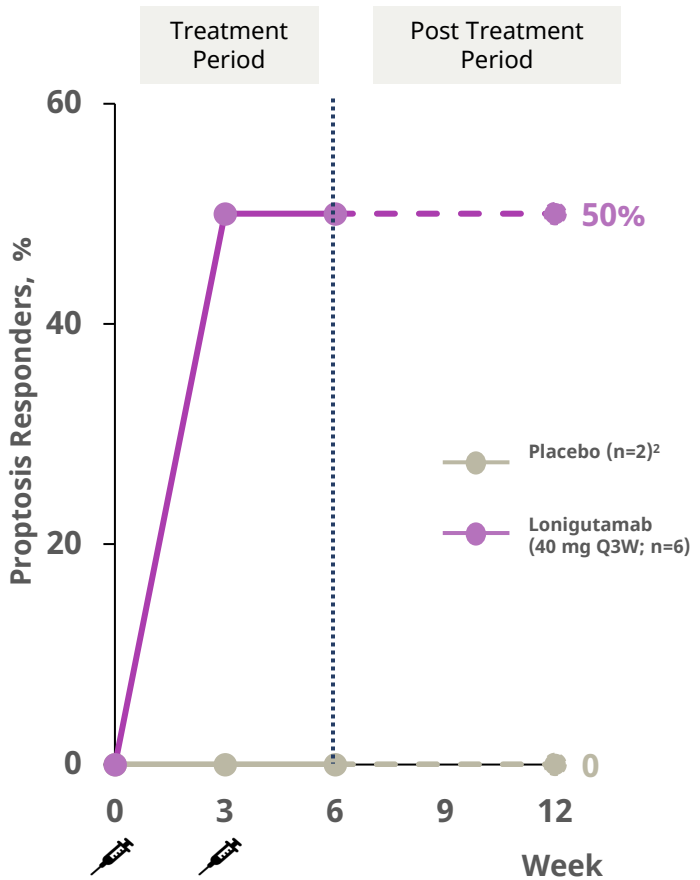
Demographics and Baseline Characteristics

	Placebo (Cohort 1) n=2[1]	Lonigutamab (Cohort 1: 40 mg Q3W) n=6
Age, mean (SD), years	49.5 (12.0)	43.8 (13.7)
Female, n (%)	2 (100.0)	5 (83.3)
White, n (%)	1 (50.0)	5 (83.3)
BMI, mean (SD), kg/m^2	28.6 (3.5)	26.6 (7.6)
Months to onset of TED, mean (SD),	14.6 (4.6)	10.2 (6.8)
Proptosis for study eye, mean (SD), mm	26.0 (0)	26.2 (2.6)
CAS total score for study eye, mean (SD)	5.5 (2.1)	4.8 (1.0)
Diplopia at baseline, n (%)	2 (100.0)	4 (66.7)

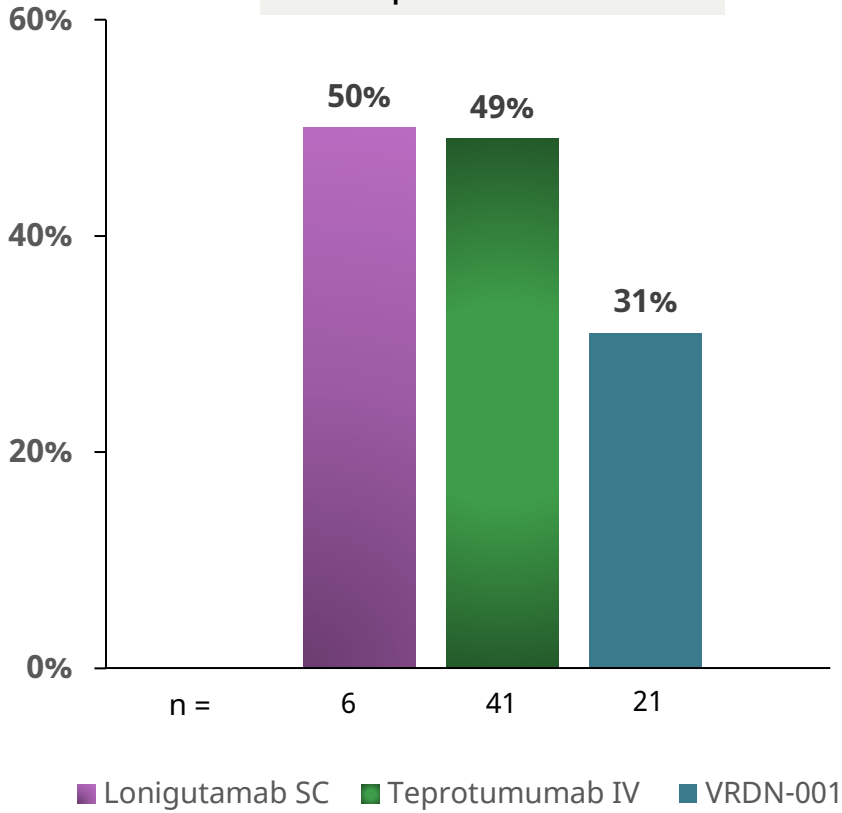
BMI, body mass index; CAS, Clinical Activity Score; Q3W, every 3 weeks; SD, standard deviation
1 One subject stopped treatment after the first dose due to AE (dysthyroid optic neuropathy, a complication from thyroid eye disease and exclusion criteria for the study) and terminated the study early due to investigator discretion. Subject was determined to be randomized to placebo following unblinding, which occurred after the final study visit for all Cohort 1 subjects.

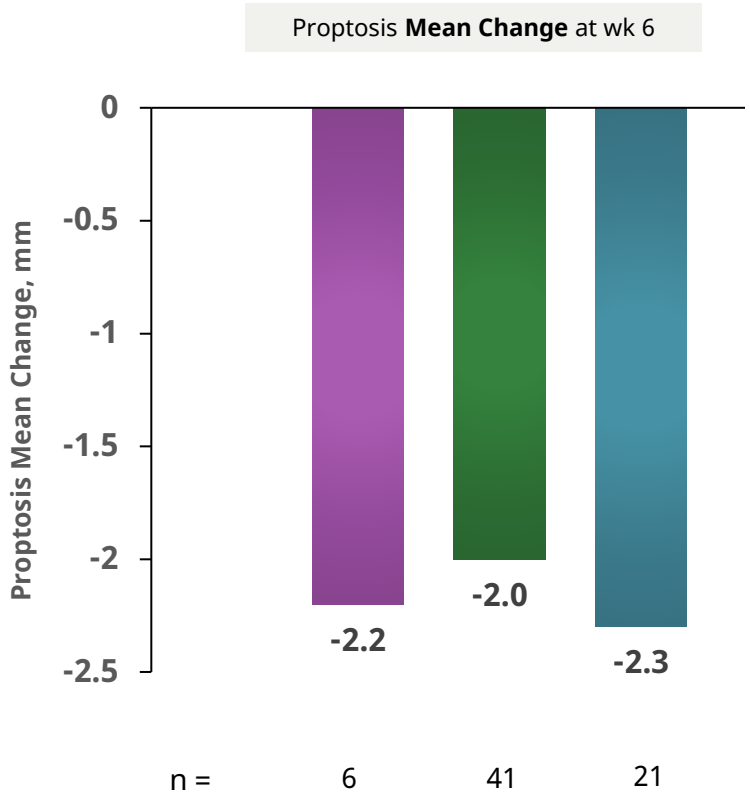
Proptosis Response Maintained Through Treatment and Post-Treatment Periods

50% of Patients Achieved Response Within 3 weeks After a Single 40mg Subcutaneous Injection



Proptosis Response[1]
(defined as ≥2-mm reduction in proptosis)

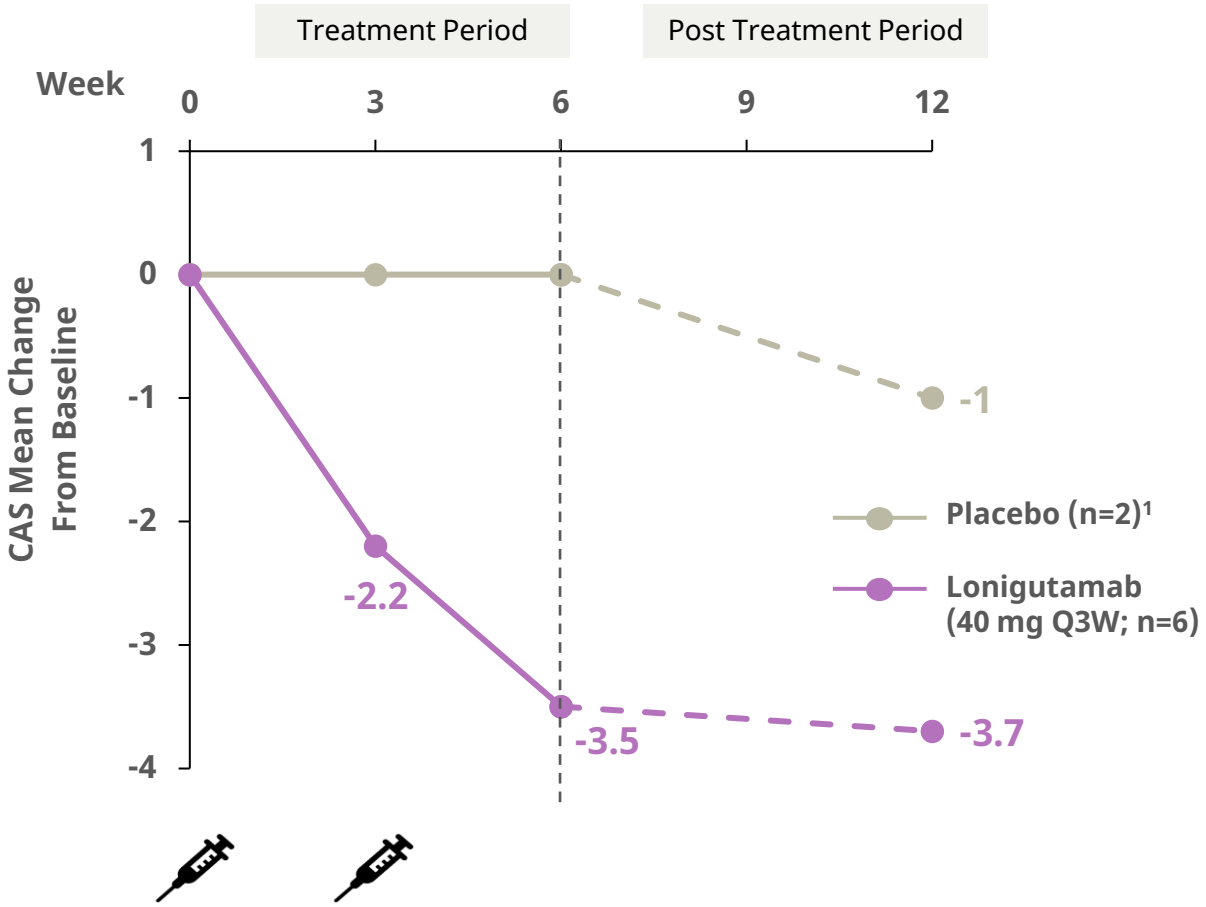


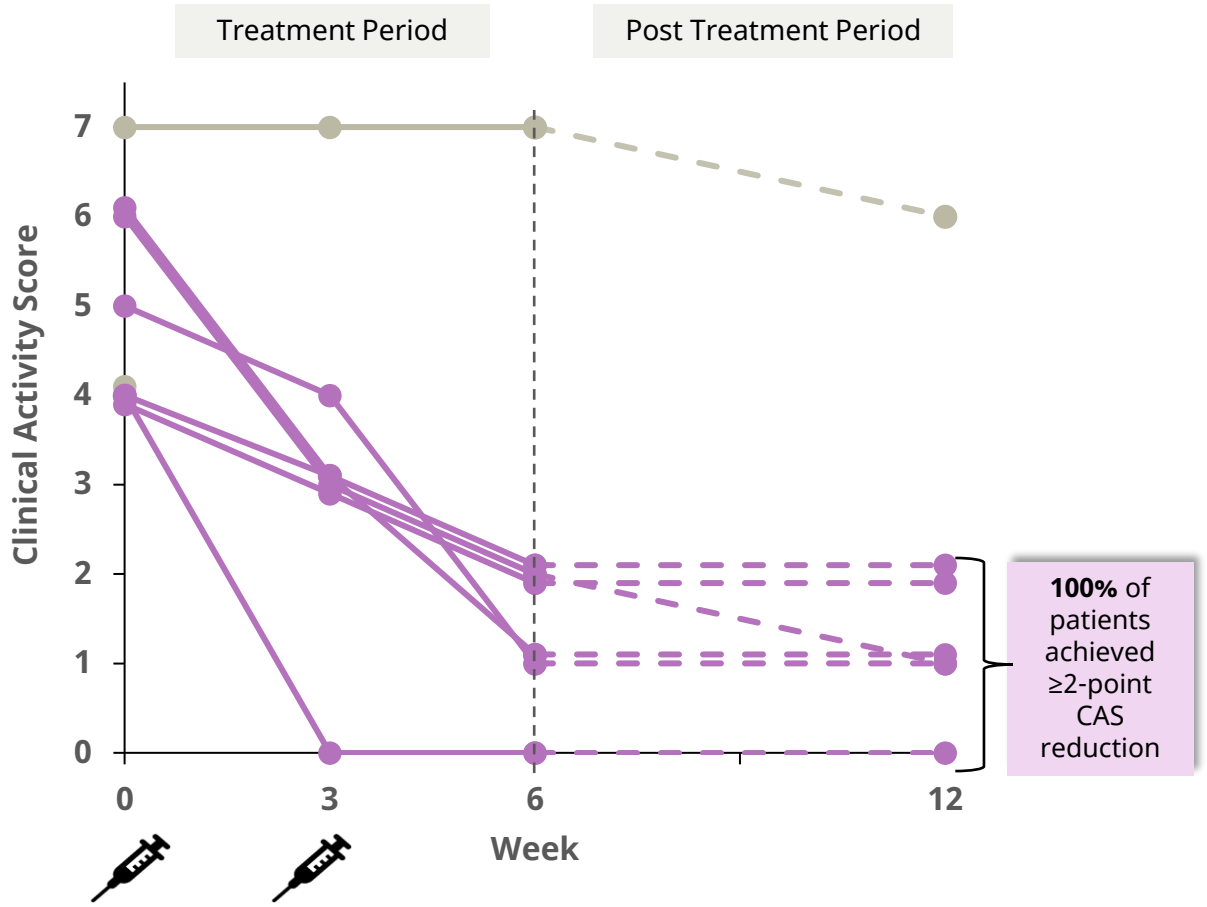


1 Proptosis was measured via Hertel exophthalmometer.
2 One patient in the placebo group had no post-baseline data and was imputed as a non responder. Q3W, every 3 weeks
3 Comparisons across trials, with inherent limitations. Not head-to-head trials. Teprotumumab data from public source: Douglas NEJM 2020 382:341:52. VRDN-001 data from public source: Kossler AAO 2023, pooled doses

Clinical Activity Score – Changes From Baseline

100% of Patients Achieved Clinically Meaningful CAS Reduction Within 6 Weeks After 2 SC Injections

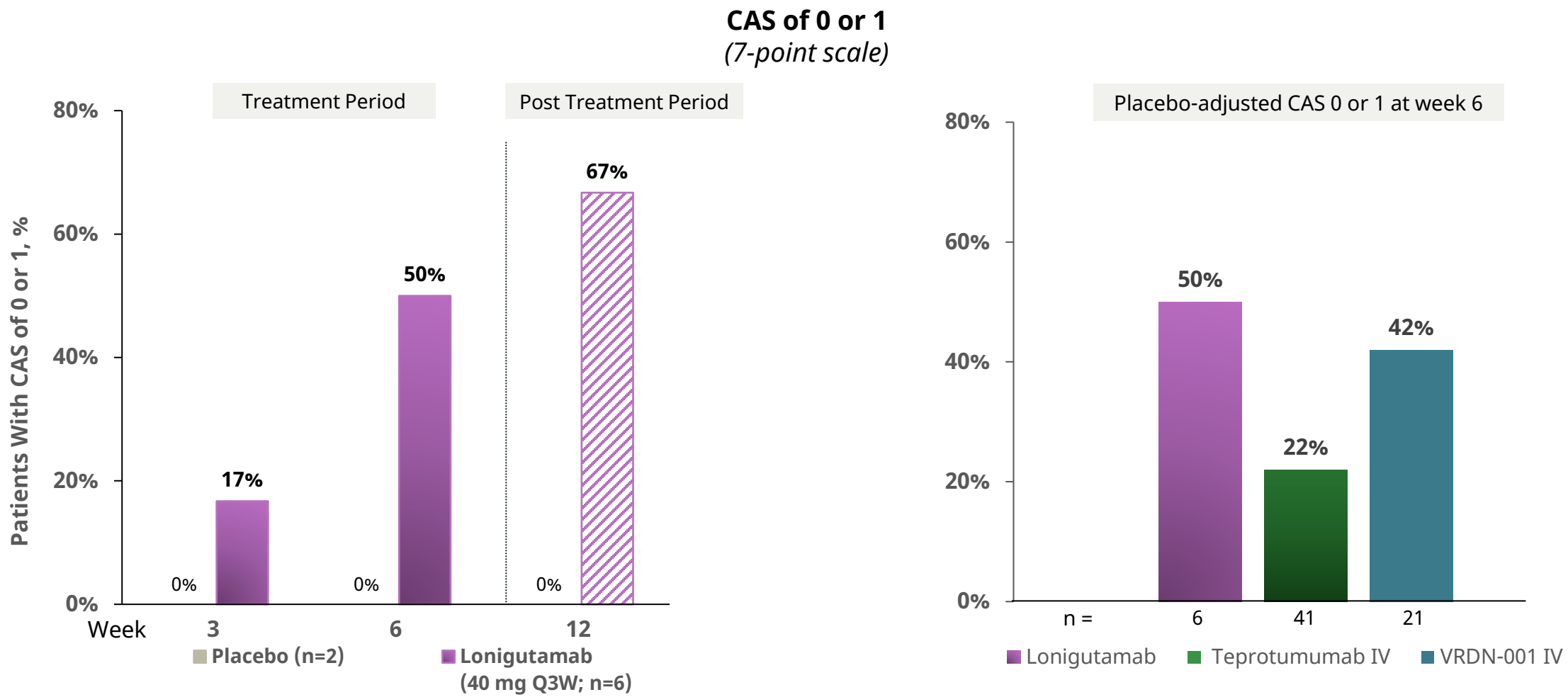




CAS Responders: patients with ≥2 pt CAS reduction considered clinically meaningful
1 One patient in the placebo group had no post-baseline data.
CAS, Clinical Activity Score; Q3W, every 3 weeks

Clinical Activity Score – 0 or 1 Through Week 12

Low Disease Activity (CAS 0 or 1) Achieved at Week 6 and Improved Over Time



One patient in the placebo group had no post-baseline data and was imputed as a non responder. Q3W, every 3 weeks
Comparisons across trials, with inherent limitations. Not head-to-head trials. Teprotumumab data from public source: Douglas NEJM 2020 382:341:52. VRDN-001 data from public source: Kossler AAO 2023.

Cohort 2: 50mg Load, 25mg QW

Open Label at 6 Weeks (n = 6)

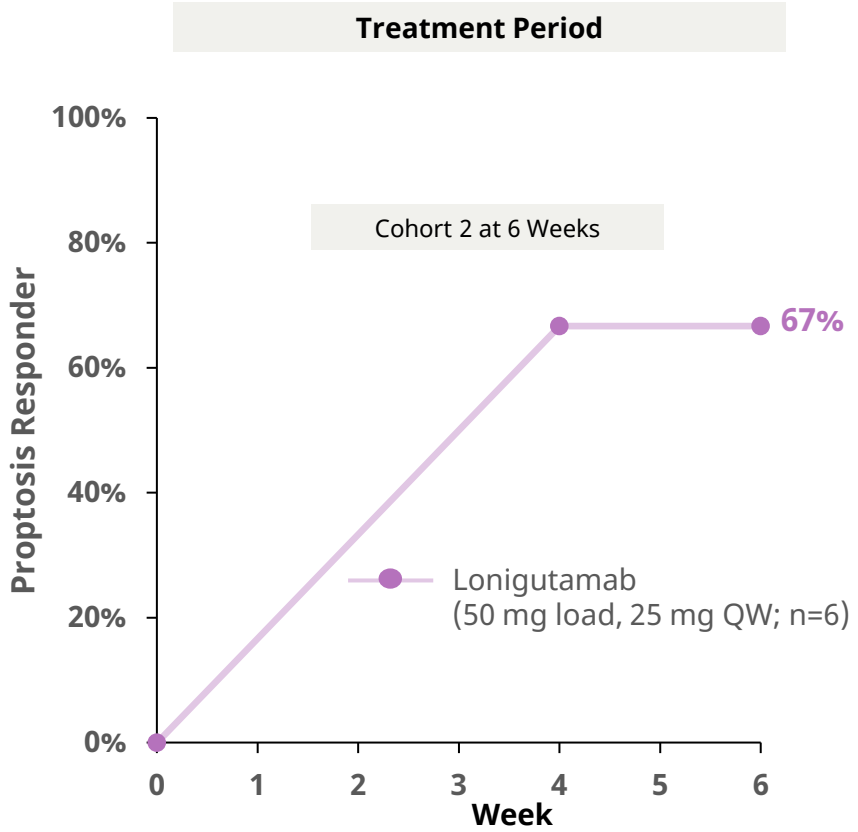
Demographics and Baseline Characteristics

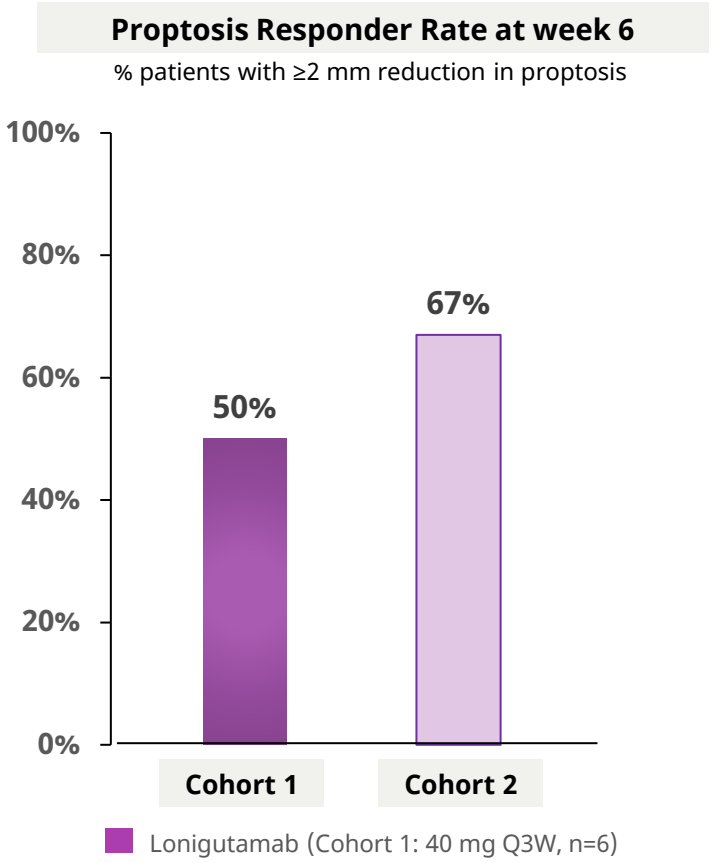
	Placebo (Cohort 1) n=2[1]	Lonigutamab (Cohort 1: 40 mg Q3W) n=6	Lonigutamab (Cohort 2: 50 mg load, 25 mg QW) n =6
Age, mean (SD), years	49.5 (12.0)	43.8 (13.7)	43.3 (13.3)
Female, n (%)	2 (100.0)	5 (83.3)	4 (66.7)
White, n (%)	1 (50.0)	5 (83.3)	2 (33.3)
BMI, mean (SD), kg/m^2	28.6 (3.5)	26.6 (7.6)	26.2 (4.1)
Months since onset of TED, mean (SD)	14.6 (4.6)	10.2 (6.8)	10.0 (4.5)
Proptosis for study eye, mean (SD), mm	26.0 (0)	26.2 (2.6)	23.2 (2.4)
CAS total score for study eye, mean (SD)	5.5 (2.1)	4.8 (1.0)	5.2 (0.75)
Diplopia at baseline, n (%)	2 (100.0)	4 (66.7)	5 (83.3)

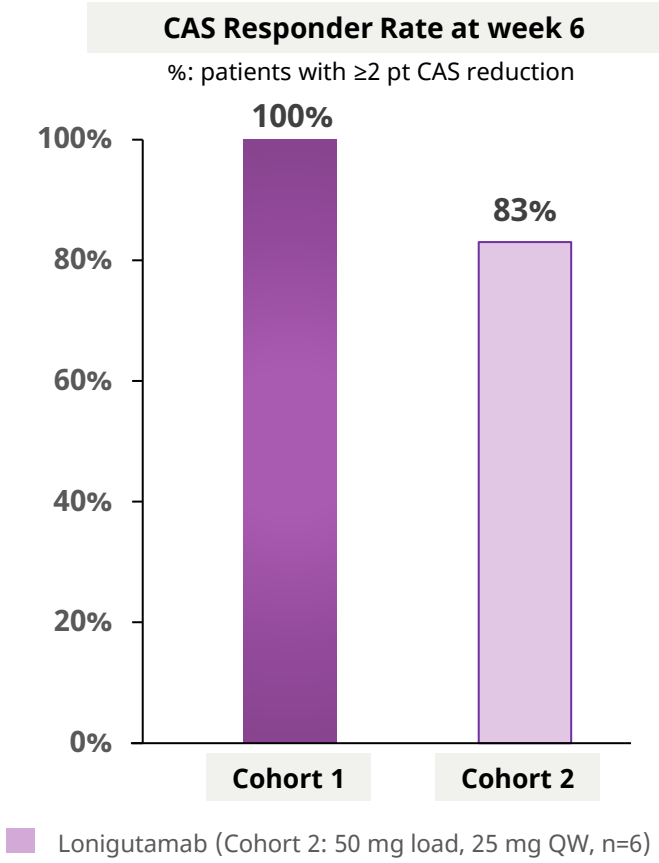
BMI, body mass index; CAS, Clinical Activity Score; Q3W, every 3 weeks; SD, standard deviation
1 One subject stopped treatment after the first dose due to AE (dysthyroid optic neuropathy, a complication from thyroid eye disease and exclusion criteria for the study) and terminated the study early due to investigator discretion. Subject was determined to be randomized to placebo following unblinding, which occurred after the final study visit for all Cohort 1 subjects. Cohort 2 demographics and baseline characteristics shown (n = 6).

Proptosis and CAS Responses Seen at Week 6

Data Consistent With Cohort 1 and Allows for Regimen Exploration

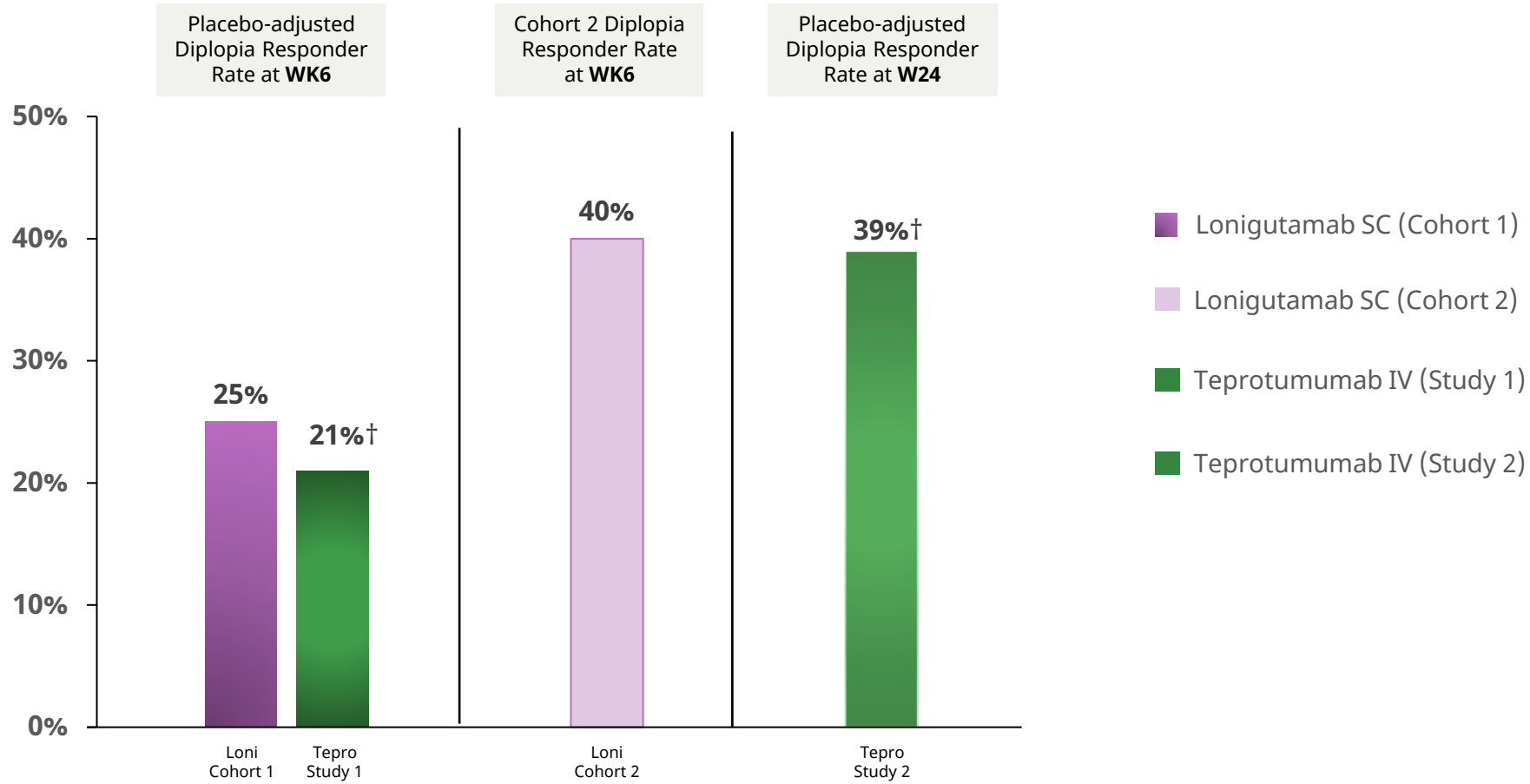






Proptosis was measured via Hertel exophthalmometer. Proptosis responder rate: % patients with ≥2 mm reduction in proptosis Q3W, every 3 weeks; QW, weekly.
CAS Responder rate: % patients with ≥2 pt CAS reduction considered clinically meaningful.

Clinically Meaningful Diplopia Responses Observed in Both Cohorts by Week 6[1]



1 Comparisons across trials, with inherent limitations. Diplopia Response defined as improvement in >1 Bahn Gorman grade.
†Teprotumumab: Ph2 Smith, et al NEJM 2017 376:1748-61, Ph3 Douglas NEJM 2020 382:341:52

Summary of Safety

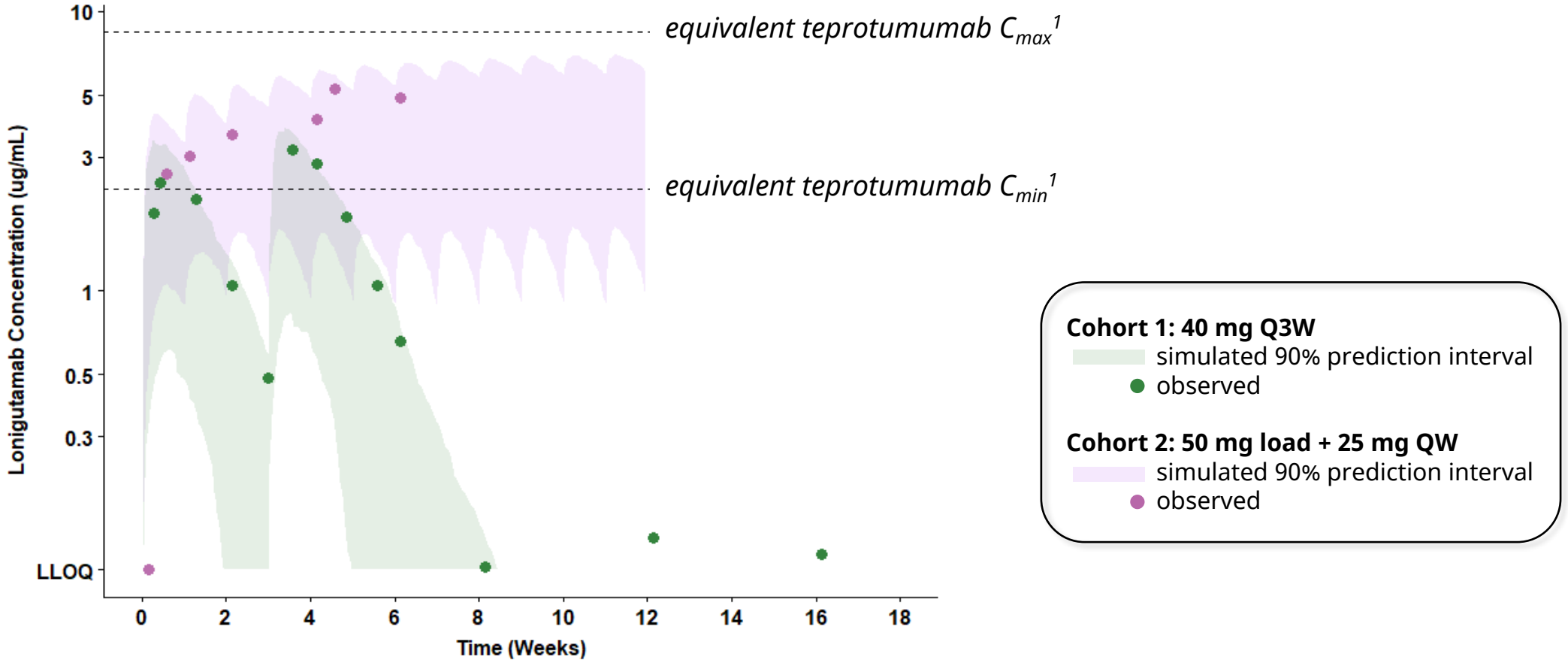
n (%)	Placebo (Cohort 1) n=2	Lonigutamab (Cohort 1: 40 mg Q3W) n=6	Lonigutamab (Cohort 2: 50 mg load, 25 mg QW) n =6
Any TEAEs	2 (100.0)	4 (66.7)	5 (83.3)
Serious	0	0	0
Any grade 2	0	1 (16.7)	2 (33.3)
Any grade 3	0	0	0
TEAEs leading to study drug discontinuation			
Optic neuropathy	1 (50.0)	0	0
TEAEs leading to death	0	0	0

- Majority of events were mild. No interruptions to study drug except the optic neuropathy in the placebo patient
- No hearing impairment, no hyperglycemia events, and no serious adverse events

Most common events (reported in 2 or more subjects on lonigutamab) were headache, injection site reactions, muscle spasms and tinnitus. Tinnitus was reported in 3 subjects all were mild and resolved without intervention. Injection site reactions were all mild. Grade 2 events included headache, joint swelling, and nausea
Q3W, every 3 weeks; TEAE, treatment-emergent adverse event; TED, thyroid eye disease.

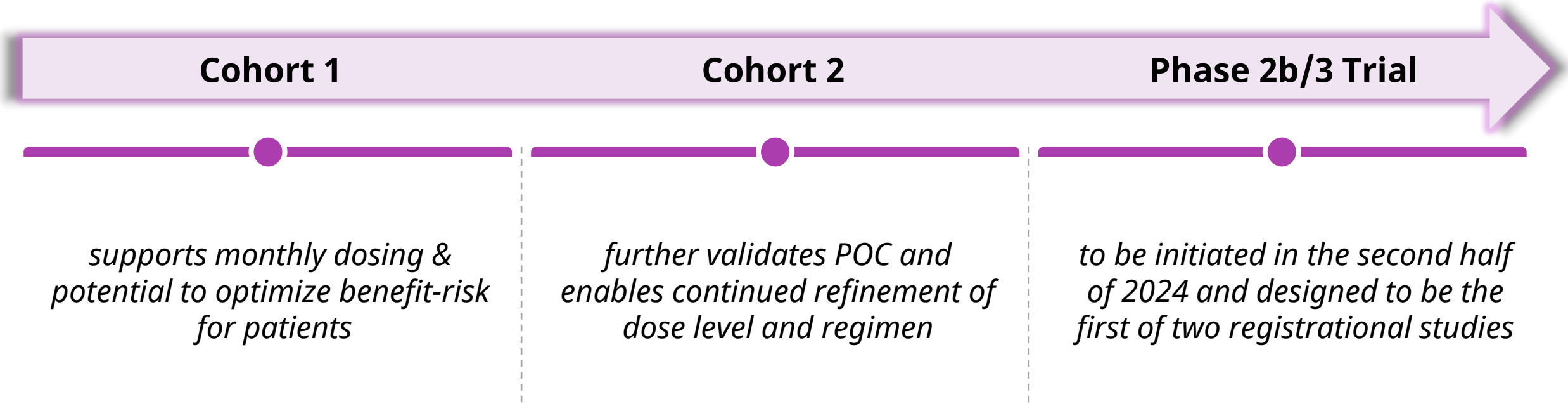
SC Exposure Achieves Responses Enabling Optimization of Benefit-Risk

Lonigutamab Achieves Robust Responses at Exposures Below Teprotumumab Cmax

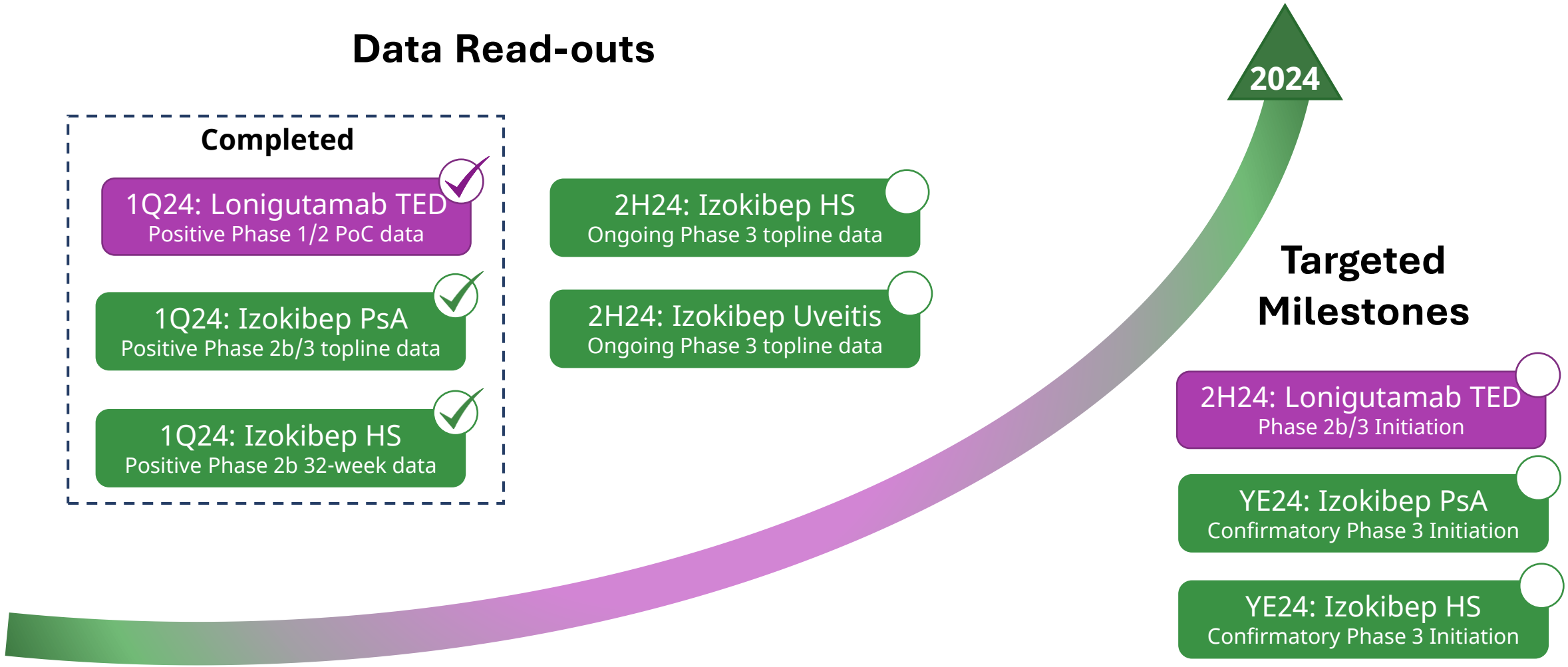


1 Comparisons across trials, with inherent limitations. Not head-to-head trials. Teprotumumab data from public source: FDA Tepezza Clinical Pharmacology review, Teprotumumab Cmax and Cmin from approved dosing regimen (10 mg/kg followed by 20 mg/kg Q3W). Equivalence calculated by ~75x scaled potency. Cohort 1: intensive sampling, Cohort 2: Cmin, through W6. LLOQ, lower limit of quantitation for the assay. Preliminary PK data from an ongoing study.

Optimizing Benefit-Risk: Improve Depth & Durability of Response, Minimize Safety Liability and Maximize Patient Convenience



Uniquely Positioned With Announcements Across Multiple Indications In 2024



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