

Corporate Presentation

August 2024





Safe Harbor Statement

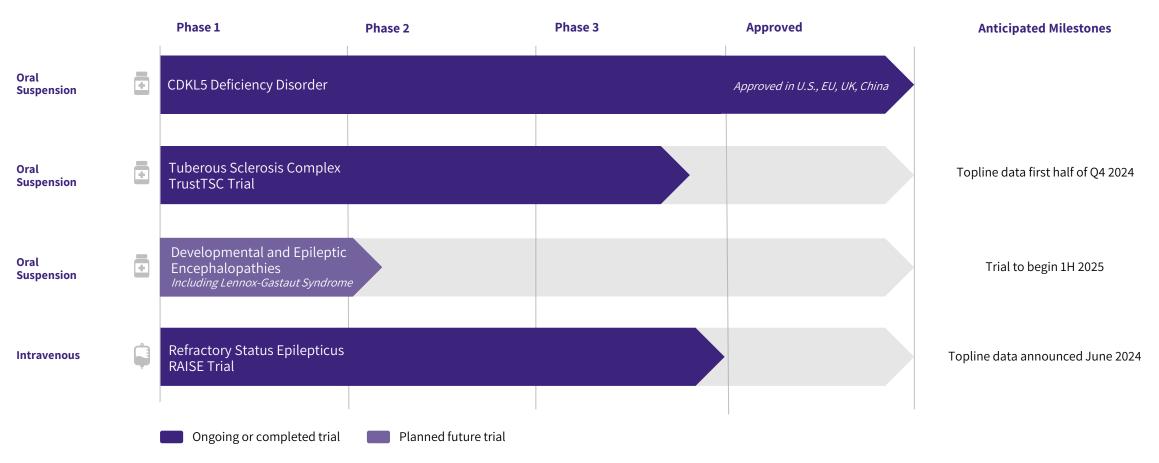
To the extent that statements contained in this presentation are not descriptions of historical facts regarding Marinus, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Words such as "may", "will", "expect", "anticipate", "estimate", "intend", "believe", and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Examples of forward-looking statements contained in this presentation include, among others, statements regarding our ability to continue as a going concern; our expected revenue and expenses; our commercialization plans for ZTALMY® and clinical development plans for ganaxolone, and the expected timing thereof; the clinical development schedule and milestones; expected dosing in our clinical trials; our expected timing to begin and complete enrollment in our clinical trials; the expected trial design, target patient population and endpoints for our clinical trials; interpretation of scientific basis for ganaxolone use; timing for availability and release of data; the potential safety and efficacy and therapeutic potential of ganaxolone; timing and expectations regarding the potential benefits ZTALMY will provide for patients and physicians; timing and expectations regarding regulatory communications and submissions; expectations regarding our agreement with BARDA; expectations regarding our current and contemplated collaborations with ex-US partners, including the potential benefits and timing thereof; expectations regarding the potential market opportunities for our product candidates; expectations regarding patient populations; expectations regarding potential commercial alliances; expectations regarding our cash flow, cash projections and cash runway; expectations regarding the continued uptake of ZTALMY; expectations regarding the impact of on-going scientific and clinical research investments on our product candidates; expectations regarding operating margins; plans for commercial investments; plans to leverage existing our infrastructure and knowledge; our plans for the global access program and the expected benefits and timing thereof; and our expectations regarding future opportunities of oral and IV ganaxolone. Forward-looking statements in this presentation involve substantial risks and uncertainties that could cause our clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties and delays relating to patient and physician acceptance of ZTALMY; our ability to obtain adequate market access for ZTALMY; our ability to comply with the U.S. Food and Drug Administration's ("FDA") requirement for additional post-market studies in the required timeframes; the timing of regulatory filings; the potential that regulatory authorities, including the FDA and the European Medicines Agency ("EMA"), may not grant or may delay approval for our product candidates; uncertainties and delays relating to the design, enrollment, completion, and results of clinical trials; unanticipated costs and expenses; early clinical trials may not be indicative of the results in later clinical trials; clinical trials results may not support regulatory approval or further development in a specified indication or at all; actions or advice of the FDA or EMA may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional clinical trials; our ability to obtain and maintain regulatory approval for our product candidates; our ability to obtain, maintain, protect and defend intellectual property for our product candidates; the potential negative impact of third party patents on our collaborators' or our ability to commercialize ganaxolone; delays, interruptions or failures in the manufacture and supply of our product candidates; the size and growth potential of the markets for our product candidates, and our ability to service those markets; our cash and cash equivalents may not be sufficient to support our operating plan for as long as anticipated; our expectations, projections and estimates regarding expenses, future revenue, capital requirements, and the availability of and the need for additional financing; our ability to obtain additional funding to support our commercial and clinical development programs; our dependence on ex-US partners to commercialize ZTALMY outside of the US; the potential for our ex-US partners to breach our collaboration agreements or terminate the agreements; and the availability or potential availability of alternative products or treatments for conditions targeted by us that could affect the availability or commercial potential of our product candidates. Marinus undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to our business in general, see filings we have made with the Securities and Exchange Commission. You may access these documents for free by visiting EDGAR on the SEC web site at www.sec.gov.



Ganaxolone Development Pipeline



Ganaxolone is a positive allosteric GABA_A receptor modulator with a well-defined MOA designed to treat patients suffering from seizure disorders. Ganaxolone is designed to modulate both synaptic and extrasynaptic GABA_A receptors to calm over-excited neurons.

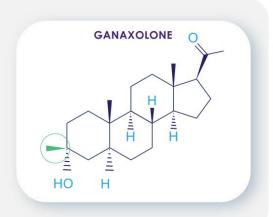






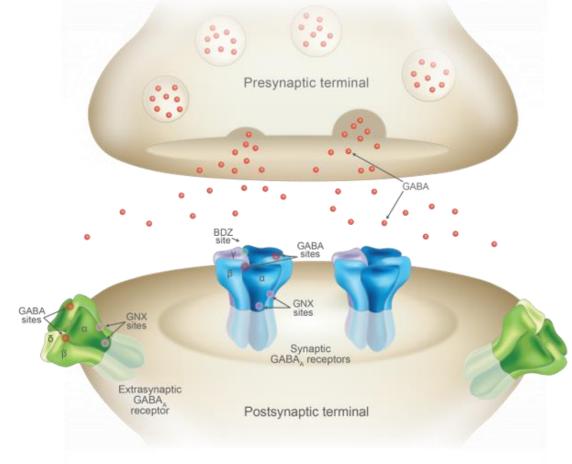
Ganaxolone Engages Both Synaptic and Extra-synaptic GABA_A Receptors

Ganaxolone is a neuroactive steroid that **targets binding sites on GABA**_A **receptors** that are distinct from the benzodiazepine site and other GABAergic molecules.¹⁻³



Ganaxolone modulates both synaptic and extrasynaptic GABA_A receptors to increase inhibitory tone¹⁻⁵

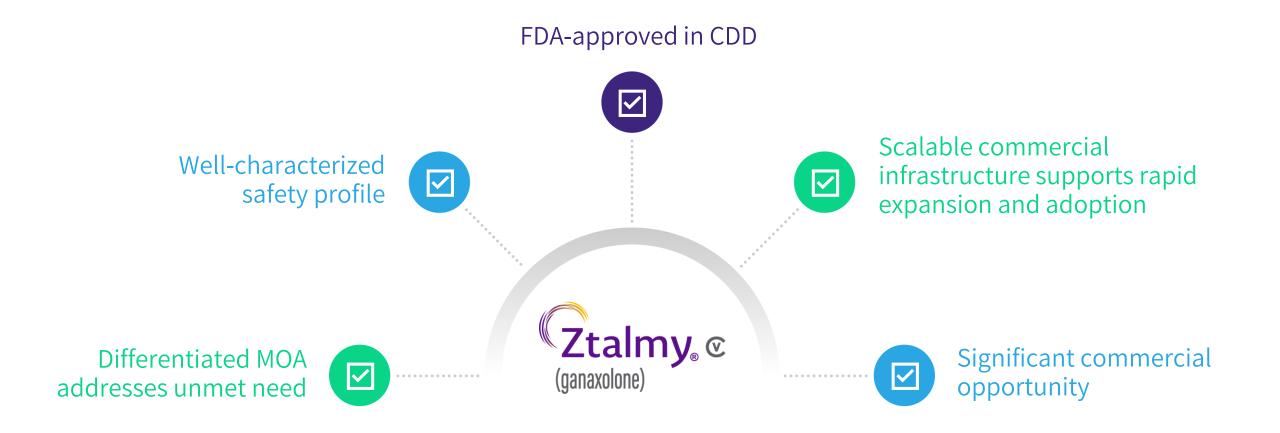
> Potentiates dual inhibitory signaling, transient (phasic) and continuous (tonic)^{1,3}







ZTALMY® Has the Potential to Significantly Advance Epilepsy Treatment





Phase 3 CDD Marigold Trial and Open Label Extension Data



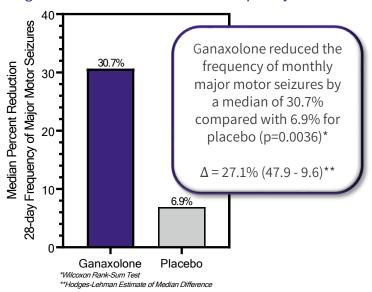




Marigold data published in The Lancet Neurology

First international CDKL5 guidelines published in Frontiers in Neurology OLE data published in *Epilepsia*

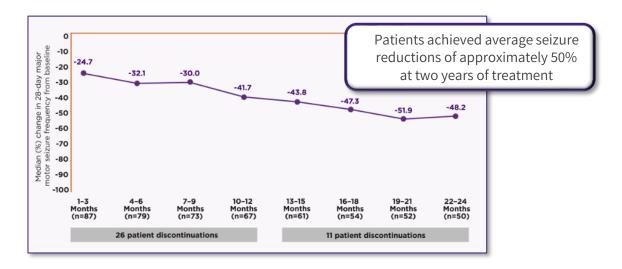
Patients taking ganaxolone experienced a significant reduction in seizure frequency



Safety Summary

- The most frequent adverse events (AEs) reported by both groups (ganaxolone vs placebo) during the double-blind were somnolence (36% vs 16%), pyrexia (18% vs 8%), and upper respiratory tract infection (10% vs 6%).
- Serious treatment-emergent AEs (TEAEs) were reported in 12% and 10% of ganaxoloneand placebo-treated patients, respectively, during the DB phase.

Reduction in monthly major motor seizure frequency through 2 years of the OLE***



Patients who remained in the clinical trial at 2 years experienced sustained reduction in MMSF1

- Following the pivotal trial, 88 out of 101 patients entered an open-label extension study to evaluate the ongoing safety and efficacy of ZTALMY.1
- The primary objective of the OLE was to collect additional safety and tolerability data. Safety findings were consistent with the double-blind phase; no new safety findings had emerged at the time of analysis. 1,2
- Additional efficacy assessments were also performed. Open-label design and small sample size preclude conclusions about efficacy.



^{2.} Specchio N, Amin S, Hulihan J, et al. Extended duration safety and efficacy of ganaxolone for the treatment of CDKL5 deficiency disorder: preliminary open-label extension analysis (Marigold Study). American Epilepsy Society. Dec 4-8, 2020. Virtual conference. Not for promotional use





ZTALMY® Performance Metrics and Growth Drivers



Net product revenue of \$8.0M for the second quarter of 2024

87% growth from Q2 2023



Full year 2024 expected net product revenue: **\$33M-\$35M**



Achieved profitability on the ZTALMY commercial investment in Q1 2024, ahead of original target



Continued strong **new patient enrollments**

Continued growth of **new prescribers driving demand**



Favorable reimbursement

dynamics across all payers, including both commercial and government programs



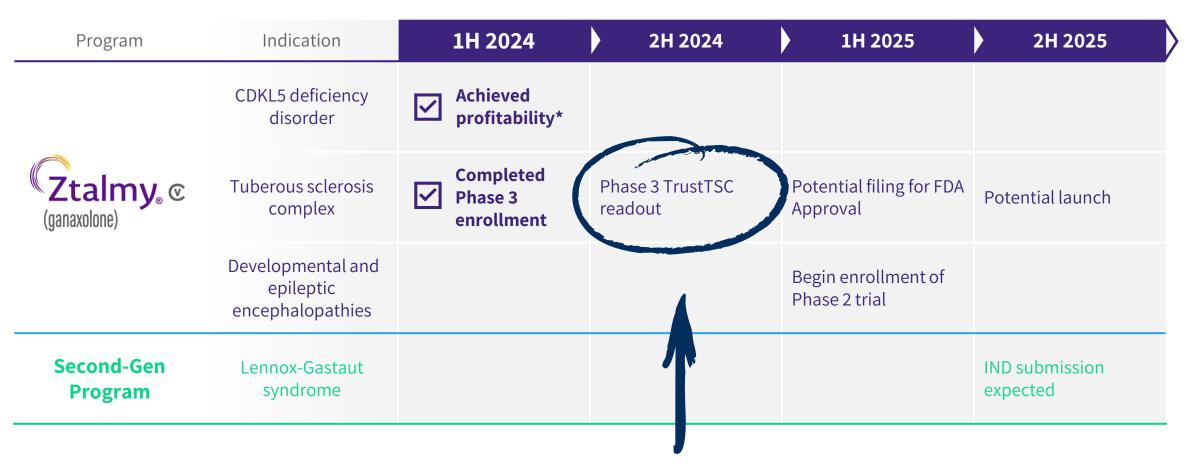
Growth Opportunities:

- >1,000 CDD patients identified through third-party data sources
- Indication expansion, including TSC
- Ex-U.S. launches (EU, MENA, China)





Significant Near-term Milestones Build on Commercial Success



Topline Data Readout Expected Before Year-End







Europe: Collaboration agreement with Orion Corporation for ganaxolone in CDD, TSC, RSE

- Up to €90 million of development, commercial, and sales milestones¹; tiered royalties in the low double-digits up to the high teens (oral suspension) and low 20s (IV)
 - Marinus is eligible to receive a €10 million payment on achievement of certain CDD launch milestones

China: Collaboration agreement with Tenacia Biotechnology for ganaxolone in CDD, TSC, SE

• Up to \$256 million of development, commercial, and sales milestones²; tiered double-digit royalties

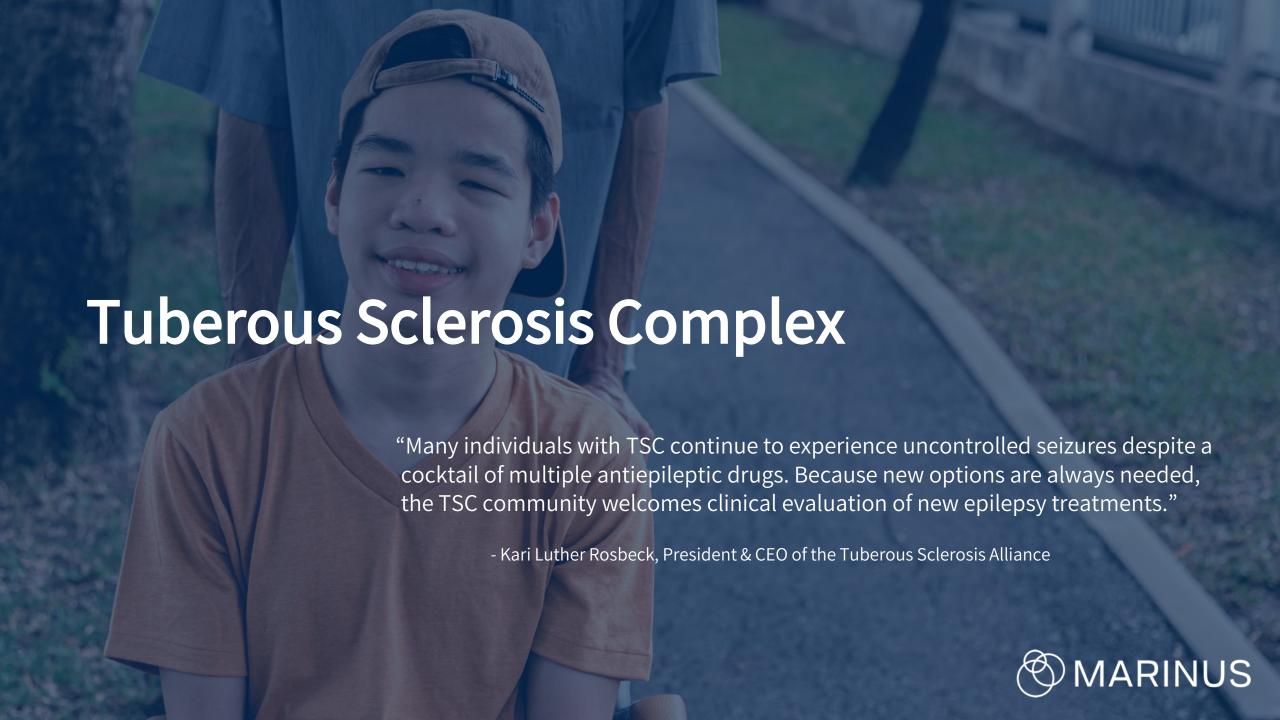
MENA: Distribution agreement with Biologix Fzco for ganaxolone

Revenue sharing arrangement with regulatory milestones

<u>Marinus Access Program:</u> Expands global access to ZTALMY in non-partnered markets for appropriate patients with seizures associated with CDD

Revenue expected beginning in Q3 2024 through distribution agreement with Uniphar Group





Tuberous Sclerosis Complex (TSC)



CAUSE \(\bigset{\bigset}{\bigset}



Defect or mutation of TSC1 and/or TSC2 genes

INCIDENCE M



~1 in 6,000 live births¹

COMMON



Seizures, cognitive impairment, behavioral difficulties, skin/kidney/lung abnormalities, etc.

EPILEPSY IN TSC



- Occurs in ~80-90% of those with TSC²
- Seizures typically begin within first year of life (infantile spasms and/or focal seizures)²

TSC is one of the most common genetic epilepsies often exhibiting highly refractory seizures despite existing therapies

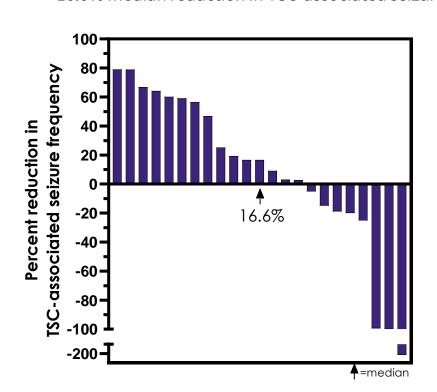


TSC Phase 2 Trial Results

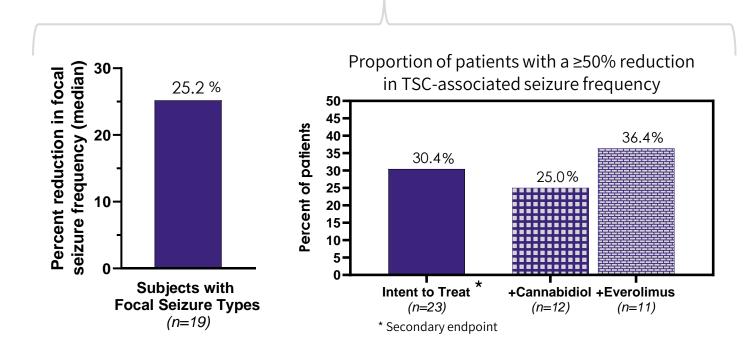


Primary Endpoint Results:

16.6% median reduction in TSC-associated seizures



Secondary and Exploratory Analyses



The most common adverse events (AEs) reported were somnolence, sedation and fatigue

17.4% (n=4) of patients discontinued due to AEs (total discontinuation rate: 26% (n=6))
74% (n=17) of patients reported somnolence-related AEs
52% (n=12) of patients required dose adjustments
One treatment-related serious adverse event (AE) of seizure was reported in the trial



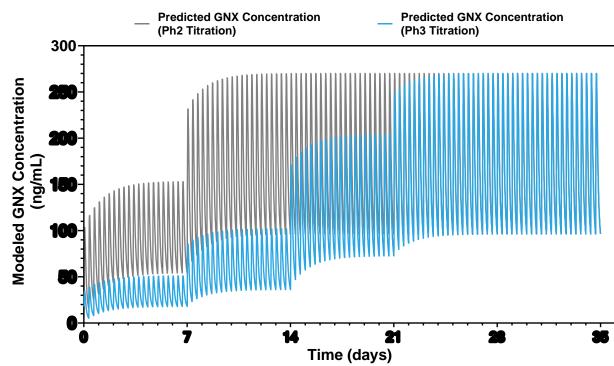
Phase 3 Protocol Refinements Informed by Phase 2 Tolerability



Phase 2
Patients without somnolence related AEs experienced greater seizure reductions

Percent reduction in TSC-associated seizure frequency (median) 20-Yes No (n=17)(n=6)

Phase 3
Slower titration initially, designed to optimize tolerability and improve efficacy

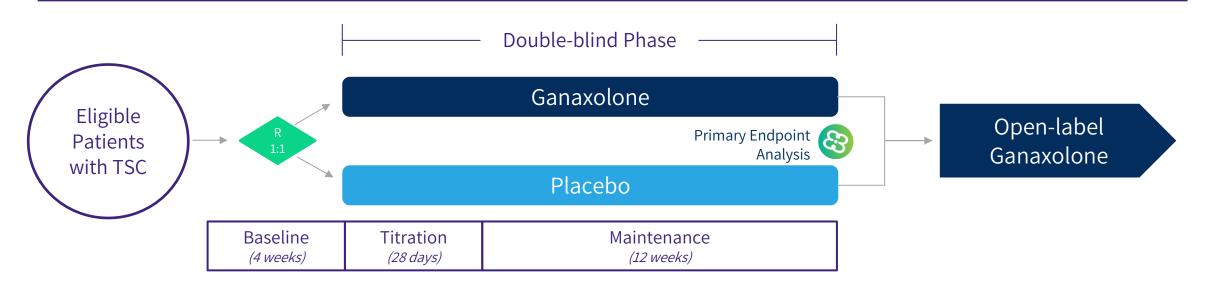


Somnolence-related AE



Phase 3 Trial Overview





- ▶ Enrollment: ~128 patients, targeting sites in the U.S., Western Europe, Canada, Israel, Australia and China
 - 90% powered to detect a 25% treatment difference
 - Statistical significance could be achieved with a treatment difference of approximately 15%
 - Similar powering assumptions and treatment group size to recent rare epilepsy trials (TSC, LGS, CDD, etc.)
- Primary Endpoint: Percent change in 28-day TSC-associated seizure frequency during 16-week treatment period compared to baseline
- ► Key Secondary Endpoints: Percent change in TSC-associated seizure frequency during 12-week maintenance period, 50% responder rate, and clinical global impression

Upcoming Milestones

- Enrollment completed mid-May; topline data expected first half of Q4 2024
- Targeting submission of a U.S. sNDA in April 2025 with a request for priority review



TrustTSC Baseline Demographics*





Failed Therapies*

(mean)

4.8

Epidiolex®/ mTor inhibitors
CBD (everolimus, sirolimus, tacrolimus)

27% 58%

<u>Age</u>

(mean [min-max])

15 [1-50]

Gender

52% 48%

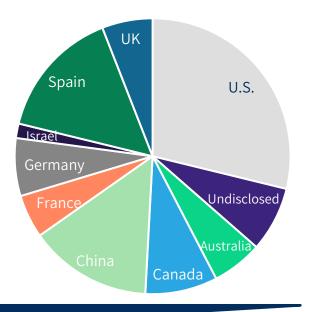
male female

Baseline Seizure Rate

(median, per 28 days)

50

Recruitment by Country



DB Discontinuation Rate**

~7%

2 discontinuations (<2%) due to somnolence-related adverse events

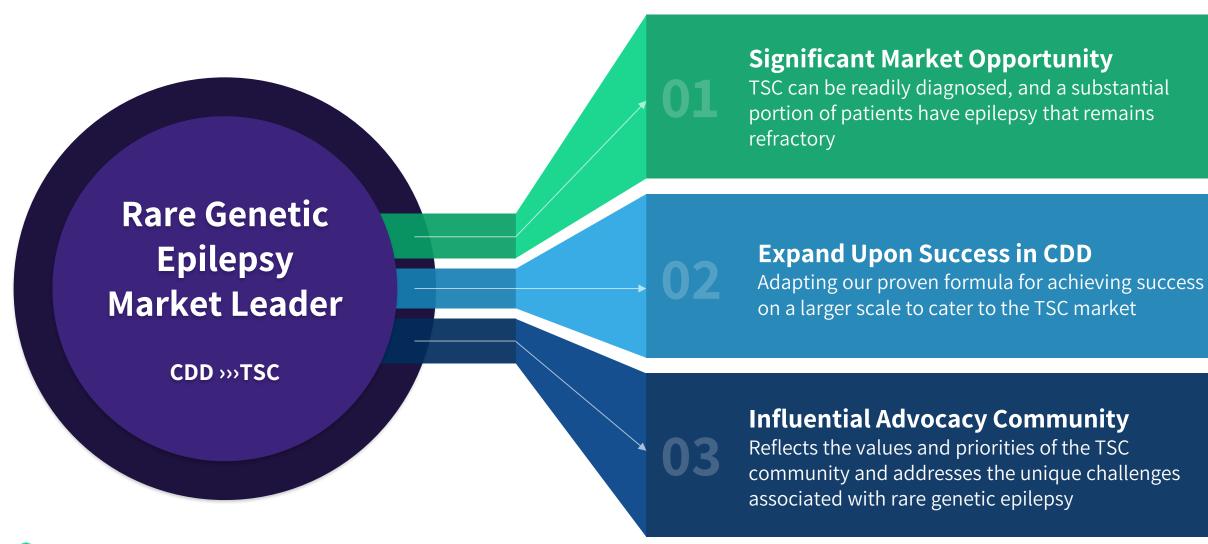
**From blinded Phase 3 trial data as of May 2024

ASM: antiseizure medication; DB: double-blind All data are preliminary and may not reflect final trial results



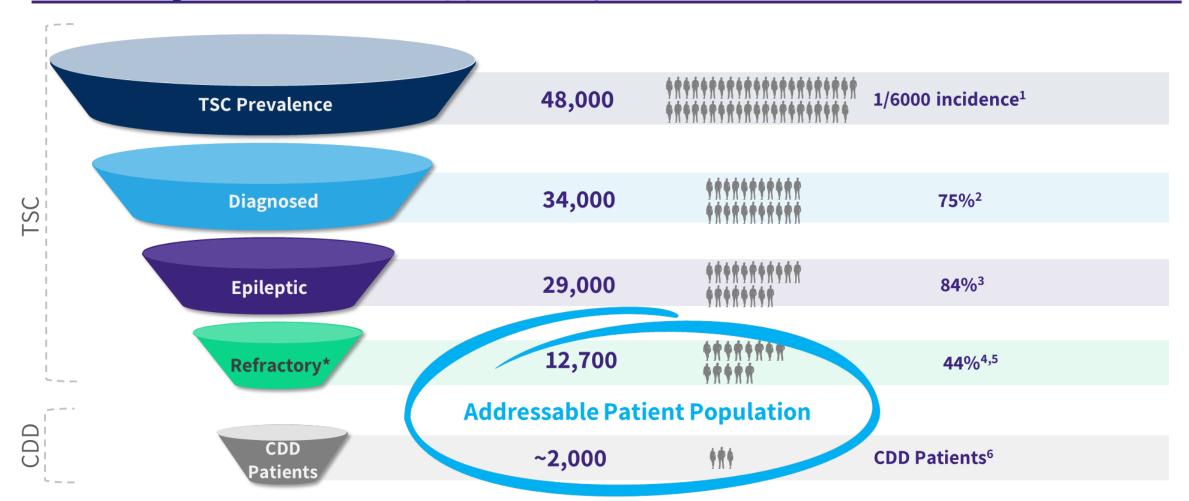
^{*}Based on enrollment as of May 2024; failed therapies includes prior and concomitant treatment

Anticipated Commercial Expansion into Tuberous Sclerosis Complex





Unlocking a 4-5x Growth Opportunity for ZTALMY® in TSC



^{*}Tried/failed 2+ antiseizure medications (Marinus' proprietary data sources)

⁶Estimated from Symonds et al. Incidence and phenotypes of childhood-onset genetic epilepsies: a prospective population-based national cohort. Brain. 2019 Aug 1;142(8):2303-2318



¹TSC Alliance; ²Marinus ZS Opportunity Assessment, 2020 Market Research; ³Curatolo P - Epilepsy in TSC: Findings from the TOSCA Study;

⁴Chu-Shore CJ et al.The natural history of epilepsy in tuberous sclerosis complex. Epilepsia.; ⁵63% (Chu-Shore) adjust -19% for Epidiolex & Afinitor Utilization 2010;

Plans to Leverage Existing ZTALMY® Infrastructure Expected to Yield Significant Returns in TSC



PATIENT IDENTIFICATION

High diagnosis rates and readily identifiable "refractory" patient populations with well established ICD-10 codes

COMMERCIAL INFRASTRUCTURE

Addition of 12-16 RAMs to reach key targets, including 17 TSC COEs

EXPANDED TARGETS

- ~50% overlap with existing CDD call points
- MSL engagements at 51% of TSC COEs/Clinics
- 40% of CDD KOLs also treat TSC

STRONG ADVOCACY PARTNERSHIPS

- Community and caregiver education
- Caregiver activation

ACCESS STRATEGY

- Expect rapid and broad payer access given reimbursement dynamics across all payers in CDD
- Protected class under Medicare Part D
- Payer channels are similar (Medicaid 45%, Medicare 20%, Commercial 35%)
- Specialty pharmacy process delivers rapid and consistent fulfillment and support

MARKET POSITIONING

Distinct TSC positioning: First Phase 3 trial with Everolimus and Epidiolex as concomitant medications

Existing ZTALMY CDD Commercial Organization



Zi ations (gana

Significant Growth Potential with Expansion into Larger Indications

Total U.S. Market Opportunity:

\$2.5B+

\$290 - 320M¹

\$2.3 - 2.5B

~2k patients in the U.S.

~12.7k refractory patients in the U.S.

CDKL5 Deficiency Disorder

Approved in U.S. in 2022

Tuberous Sclerosis Complex

Potential U.S. Approval 2025

~48k patients in the U.S.

Lennox-Gastaut Syndrome

Broad potential in refractory epilepsies

Developmental and Epileptic Encephalopathies

^{2.} Assumes average TSC patient dosed at ~15 - 20% higher than CDD (based on Phase 2 trial data)



^{1.} Based on an average Ztalmy daily dose of approximately 1,150 - 1,200 mg/day (internal estimate based on 1H 2024 actual results)



Second Generation Ganaxolone - Prodrug



Goals



Increase efficacy

Consistent delivery to achieve target plasma concentration



Improve tolerability

Optimize PK profile to reduce Cmaxrelated adverse effects



Reduce dosing frequency

More sustained exposure to allow once- or twice-daily dosing



Lower cost of goods

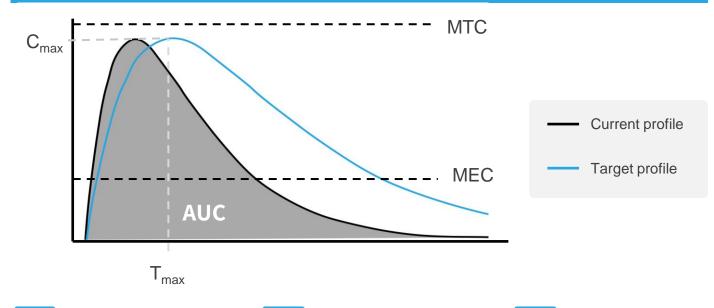
Better absorption to reduce API requirements per dose



Enhance IP protection

Improve formulation characteristics to provide opportunity for new IP

Target Oral Pharmacokinetic Profile







Increase the proportion of time the plasma level exceeds a minimally effective concentration (MEC)

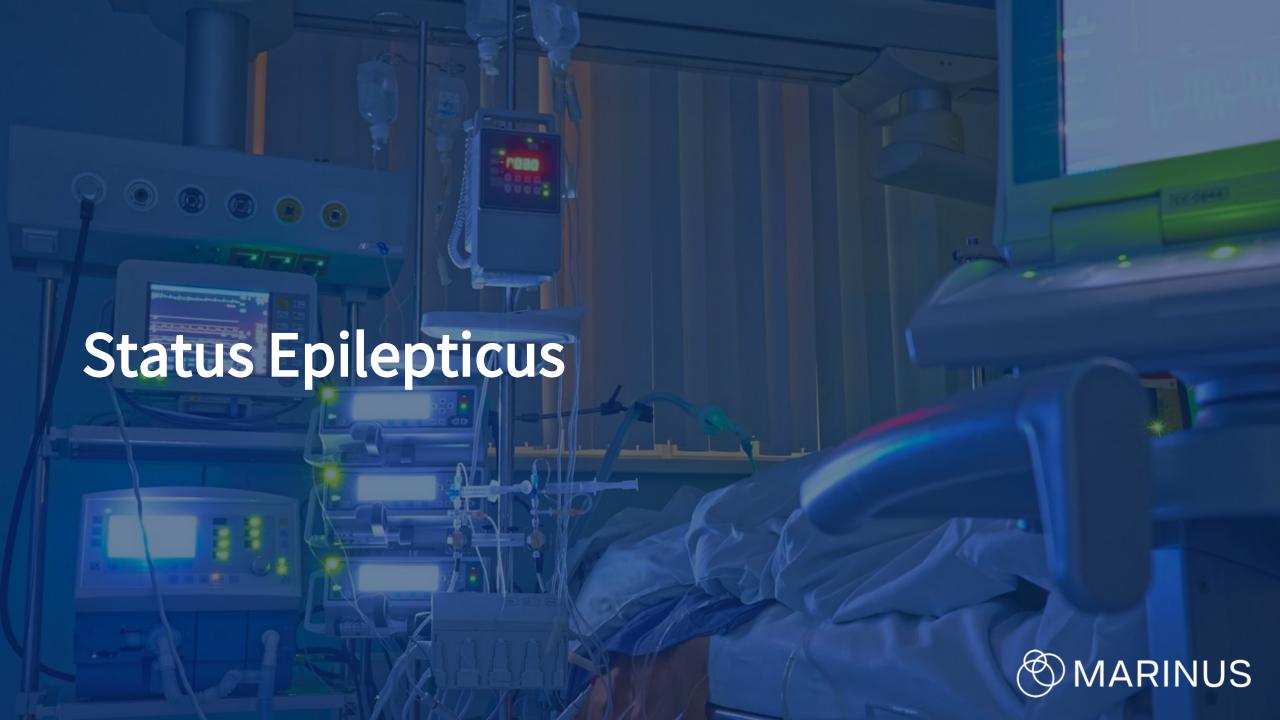


Avoid a significant increase in peak level (C_{max}) that would exceed the maximum tolerated concentration (MTC)



- Prodrug of ganaxolone in development
- **IND** submission targeted Q4 2025





Status Epilepticus Overview



Status =

Condition resulting from either the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms which lead to:

- abnormally prolonged seizures (after time point t₁)
- can have long-term consequences (after time point t₂)



Incidence of SE in the United States:

~150,000

SE episodes per year¹



Associated with significant morbidity:

- Disabling cognitive deficits²
- Increased risk for development of epilepsy²



Increased mortality associated with:

- Underlying SE etiology³
- More refractory SE⁴
- Therapeutic coma exposure³
- Increased age³

\$

Significant healthcare utilization:

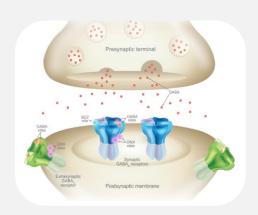
 Substantial direct healthcare cost⁵ especially as SE progresses⁶

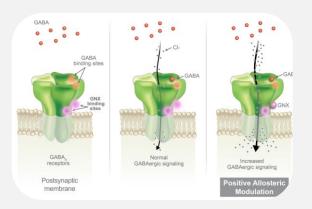


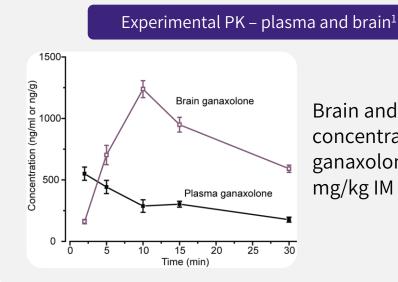
Pharmacokinetics/Pharmacodynamics Well Suited for Acute SE Treatment



Ganaxolone activates the extrasynaptic GABA_A receptor, is associated with high brain concentrations, and delivers a rapid onset of action.







Brain and plasma concentration after ganaxolone 3 mg/kg IM in mice

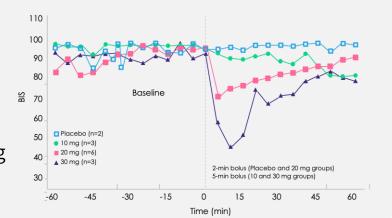
Human PK²

Following 30 mg ganaxolone bolus (over 5 minutes):

> C_{max} 1,240 ng/mL T_{max} 0.08 hrs



EEG bispectral index in healthy volunteers following IV ganaxolone





Zolkowska D, Wu CY, Rogawski MA. Intramuscular allopregnanolone and ganaxolone in a mouse model of treatment-resistant status epilepticus. Epilepsia. 2018 Oct;59:220-7.

Data on file, Marinus Pharmaceuticals, inc.

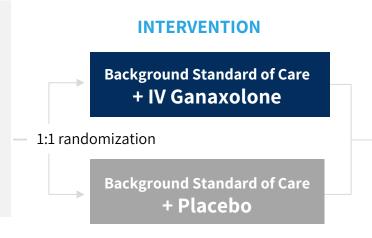
RAISE: Phase 3 Trial in Refractory Status Epilepticus



STUDY POPULATION

Status epilepticus patients aged ≥12 years who have failed 2 or more antiseizure treatments for the acute treatment of SE*





CO-PRIMARY ENDPOINTS

Onset of Action: Proportion of patients with SE cessation within 30 minutes

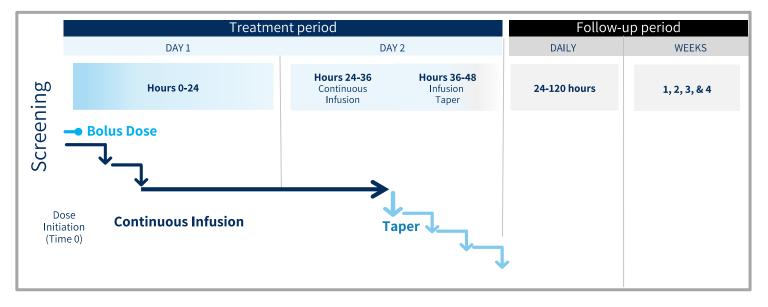
Durability of Effect: Proportion of patients with **no progression to IV anesthesia for 36 hours**

KEY SECONDARY ENDPOINTS

Onset of Action: Time to SE cessation

Durability of Effect: No progression to IV anesthesia for 72 hours

DOSING REGIMEN





RAISE Topline Results: Baseline Characteristics



Baseline Characteristics*	Placebo (n = 49)	IV Ganaxolone (n = 51)
Age (years), median (range)	59 (15 – 90)	60 (16 – 88)
Male sex, no. (%)	30 (61.2)	30 (58.8)
Mechanical ventilation prior to IP initiation, no. (%) ^A	18 (38.3)	21 (42.9)
Baseline STESS score, median (IQR) Score 0-2, no. % (Favorable) Score 3-6, no. % (Unfavorable)	3 (1, 4) 22 (44.9) 25 (51.0)	3 (2, 5) 14 (27.5) 34 (66.7)
Unknown	2 (4.1)	3 (5.8)
Number of failed ASMs, mean (SD)	3.1 (1.3)	3.4 (1.7)
Seizure burden (%), mean (SD)	30 (30)	37 (32)
Duration of status epilepticus (hr), mean (SD)	32.8 (35.6)	42.4 (58.5)

Baseline Characteristics* Continued	Placebo (n = 49)	IV Ganaxolone (n = 51)
Status epilepticus subtype – %		
With prominent motor symptoms	11 (22.4)	15 (29.4)
Without prominent motor symptoms	38 (77.6)	35 (68.6)
Primary etiology of status epilepticus		
Exacerbation of underlying epilepsy	21 (42.9)	15 (29.4)
ICH or IVH	5 (10.2)	4 (7.8)
Head trauma	5 (10.2)	3 (5.9)
Ischemic stroke	3 (6.1)	4 (7.8)
Cerebral tumor	3 (6.1)	12 (23.5)
CNS infection	1 (2.0)	4 (7.8)
Inflammation/autoimmune disease	0 (0)	2 (3.9)
Other	3 (6.1)	4 (7.8)
Unknown	8 (16.3)	3 (5.9)

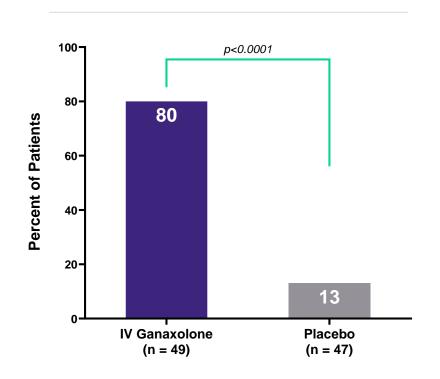
^{*}Safety population (unless otherwise noted) AITT population



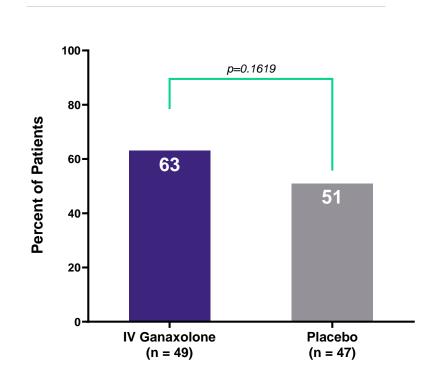
RAISE Topline Results: Co-Primary Endpoints



Proportion of patients with SE cessation within 30 minutes without medications for the acute treatment of SE



Proportion of patients with no progression to IV anesthesia for 36 hours



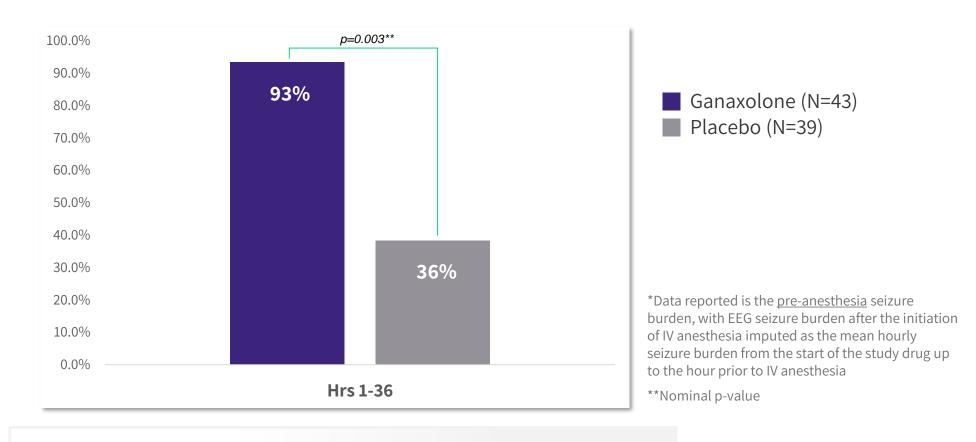
The incidence of serious adverse events was similar between the treatment and placebo arms (n=19 for IV ganaxolone, n=18 for placebo), with hypotension being more commonly seen in the IV ganaxolone arm.



RAISE Topline Results: EEG Secondary Endpoint



Median percent reduction in EEG seizure burden*



EEG seizure burden is a potential measure of durability of effect

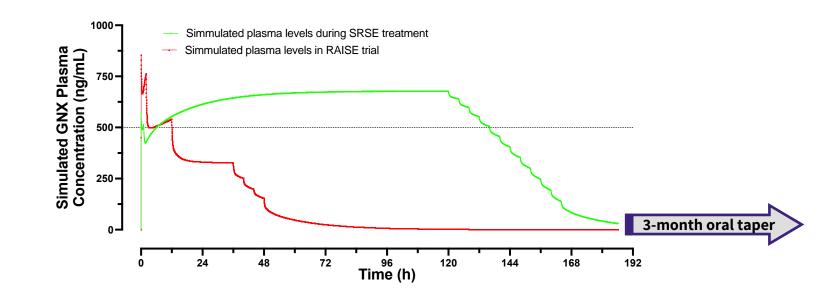






31 patients with SRSE treated with IV ganaxolone as of August 2024 14 with regimen similar to RSE dosing 17 with new regimen specific to SRSE

- SRSE-specific dosing approach
 - ↓Cmax but ↑ AUC
 - 3-month oral wean
 - Ganaxolone 833mg/day x48h → 1,050mg/day x 168h
 - Captisol® 50gm/day → 63gm/day







Financial Overview



2024 Full Year Guidance

	<u>Actual</u>	<u>Guidance</u>	
	1H 2024	2H 2024	
ZTALMY Net Revenue	\$15.5 million	\$17.5 - \$19.5 million	
SG&A & R&D ¹	\$80.3 million	\$55 - \$60 million	
SBC ²	\$9.8 million	~\$10 million	

Financial Summary (at June 30, 2024):

- \$64.7 million in cash and cash equivalents
- \$60 million in debt, matures in June 2026
 - Estimated 2H 2024 principal and interest payments of \$7.3 million
- 55.0 million shares outstanding; 68.4 million shares outstanding on a fully dilutive basis³

Nasdaq: MRNS

Analyst Coverage*:

Cantor Fitzgerald: Charles C. Duncan, Ph.D.

T.D. Cowen: Joseph Thome, Ph.D.

H.C. Wainwright & Co: Douglas Tsao

Jefferies: Andrew Tsai

JMP Securities: Jason N. Butler, Ph.D.

Ladenburg Thalmann: Michael Higgins

Oppenheimer: Jay Olson

RBC: Brian Abrahams

RW Baird: Brian Skorney

Leerink Partners: Marc Goodman

Truist: Joon Lee, M.D., Ph.D.



¹Reflects combined SG&A and R&D expenses.

² Non-cash Stock-Based Compensation (SBC) expense, included in note (1).

³ Fully dilutive total includes impact of pre-funded warrants and outstanding stock options and RSU's

^{*}Note: Opinions, estimates, and forecasts of the individual analysts regarding Marinus do not represent opinions, estimates, and forecasts of Marinus. The listing above does not imply endorsement or concurrent with their information, conclusions, or recommendations.





Multiple Layers Of Potential Protection

U.S. Patents/ Patent Applications Expiration Date

Status Epilepticus				
Method of Use	Patent granted on clinical regimen	2040		
	Patent granted on clinical regimen using broader ganaxolone dosing	2040		
	Applications pending on dosing regimens for SRSE and ESE	2041/2042		
Formulation	Licensed Captisol® patents	Through 2033		
romatation	Applications pending on IV formulation	2036		
CDKL5 Deficiency Disorder				
Method of Use	Patent granted (licensed) for method of treating CDKL5 deficiency disorder	2037		
	Application pending on dosing regimen	2038/2041/2042		
Formulation	Patents granted (oral suspension)	2031 (if PTE granted)		
Tuberous Sclerosis Complex				
Method of Use	Two patents granted for method of treating TSC-related epilepsy	2040		
	Application pending on new dosing regimens	2041/2042		
Formulation	Patents granted (oral suspension)	2031 (if PTE granted)		
Second Generation Ganaxolone				
Formulation	Application pending on second generation formulations	2042/2043		





Appendix



A Comprehensive Commercial Strategy to Grow the ZTALMY® Brand





Patient identification

- Elevate by educating HCPs on the importance of determining the genetic etiology of patients with refractory epilepsy syndromes
- Increased investment in third party data expected to allow targeting of approximately 2x more CDD patients



Activate the caregiver community

 Inspire through newly added "Shining Moments™" educational programing delivered directly to the caregiver community focused on ZTALMY and CDD the community

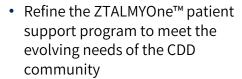


Focused education to **HCPs to establish ZTALMY** as the standard of care for **CDD** seizure management

- Promotional education targeted to HCPs with a high propensity of having CDD patients and prescribing ZTALMY
- Data driven analytics and HCP segmentation strategies to deliver the right message, to the right HCP, at the right time



Continuously enhance the patient experience



Drive best in class practices, establish Marinus as a leader in refractory epilepsy, and build capabilities for future launches

Not for promotional use



Average Ganaxolone Levels Correlate with Seizure Reduction





- Logarithms of plasma ganaxolone level and percentage change in major motor seizure frequency were negatively correlated
- Patients in the Medium and High ganaxolone level groups had an average ganaxolone concentration of 120 ng/mL and a median 38.5% reduction in seizure frequency
- Incidence of CNS-related adverse events was similar across ganaxione dose level groups

Equivalent GNX Level (ng/mL) Equivalent Log_e Percent Change Major Motor **Motor Seizure Frequency** r = -0.512p = 0.001Seizure Change 4.0 3.5 in Majo 3.0 3.0 6.0 Loge GNX Level (ng/mL) *Pearson correlation

Goal of reformulation is to drive consistent plasma ganaxolone levels to the mid- and upper-end of the target range

