Corporate Presentation

November 2024



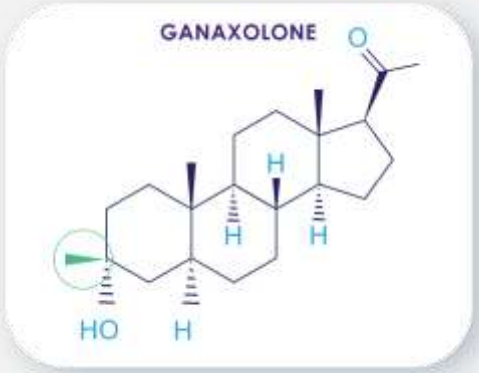
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To the extent that statements contained in this presentation are not descriptions of historical facts regarding Marinus, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor 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 expectations regarding the review and exploration of strategic alternatives and their potential impact on stockholder value; our expectations regarding the future of the company’s operations; our net product revenue and other financial guidance and projections; statements regarding our expected clinical development plans, enrollment in our clinical trials, and regulatory communications, and the timing thereof; our expected cash runway; our expectations and beliefs regarding the FDA and EMA with respect to our product candidates; our expectations regarding our cost reduction plans; the potential safety and efficacy of ganaxolone; and other statements regarding the company's future operations, financial performance, financial position, prospects, objectives and other future event. 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, the risk that exploration of strategic alternatives may not result in any definitive transaction or enhance stockholder value and may create a distraction or uncertainty that may adversely affect our operating results, business, or investor perceptions; uncertainties regarding future costs and expenses; Marinus’ ability to continue as a going concern; Marinus’ ability to maintain compliance with its debt covenants and risks and uncertainties regarding the ability to do; unexpected market acceptance, payor coverage or future prescriptions and revenue generated by ZTALMY; the pricing and reimbursement process can be time consuming and may delay commercialization of ZTALMY in one or more European countries; our dependence on Orion to commercialize ZTALMY in Europe pursuant to the exclusive collaboration agreement; unexpected actions by the FDA or other regulatory agencies with respect to our products; competitive conditions and unexpected adverse events or patient outcomes from being treated with ZTALMY, the company’s cash and cash equivalents may not be sufficient to support its operating plan for as long as anticipated; our ability to comply with the FDA’s requirement for additional post-marketing studies in the required time frames; the size and growth potential of the markets for the company’s products, and the company’s ability to service those markets; the company’s expectations, projections and estimates regarding expenses, future revenue, capital requirements, and the availability of and the need for additional financing; delays, interruptions or failures in the manufacture and supply of our product; the company’s ability to obtain additional funding to support its programs; and the company’s ability to protect its intellectual property. 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.

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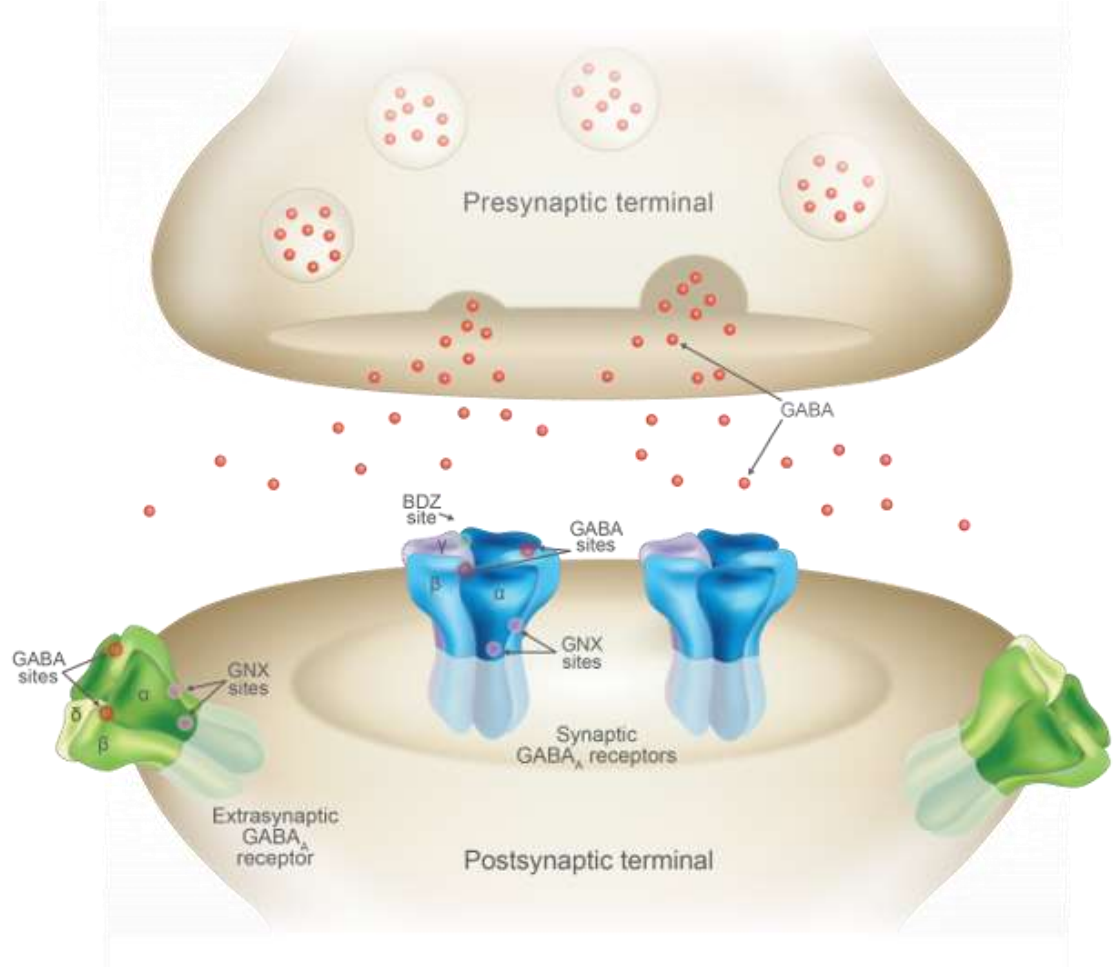
Ganaxolone Engages Both Synaptic and Extra-synaptic $GABA_A$ Receptors

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 tone[1-5]

- **Potentiates dual inhibitory signaling, transient (phasic) and continuous (tonic)[1,3]**



BZD, benzodiazepine; GNX, ganaxolone

1. Reddy DS and Woodward R. *Drugs Fut.* 2004;29(3):227-242. 2. Reddy DS, Estes WA. *Trends Pharmacol Sci.* 2016;37(7):543-561. 3. Carver CM, Reddy DS. *Psychopharmacology (Berl).* 2013;230(2):151-188. 4. Reddy DS. *Front Cell Neurosci.* 2013;7:115. 5. Reddy DS, Rogawski MA. Jasper's Basic Mechanisms of the Epilepsies [Internet]. 4th edition; **6.** Paul SM, Purdy RH. *Neuroactive steroids*, Faseb J 1992; 6(6):2311-22.

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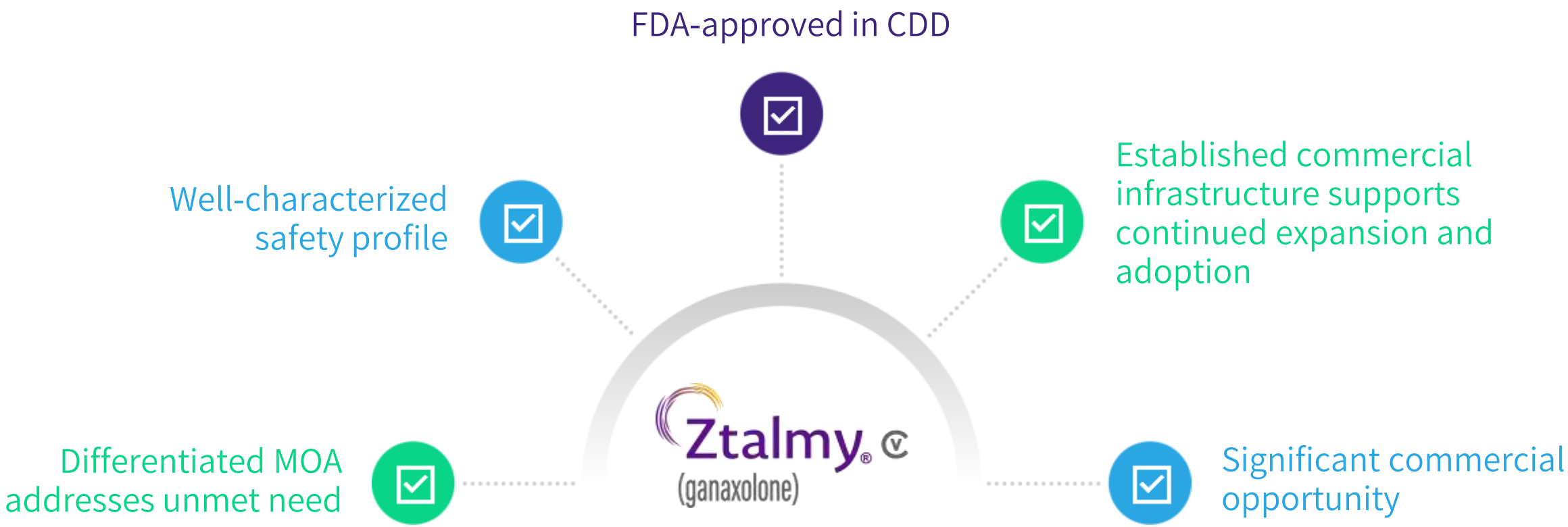


ZTALMY® Clinical and Commercial Overview

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ZTALMY® Has the Potential to Significantly Advance Epilepsy Treatment



CDD: CDKL5 deficiency disorder; MOA: mechanism of action

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Phase 3 CDD Marigold Trial and Open Label Extension Data

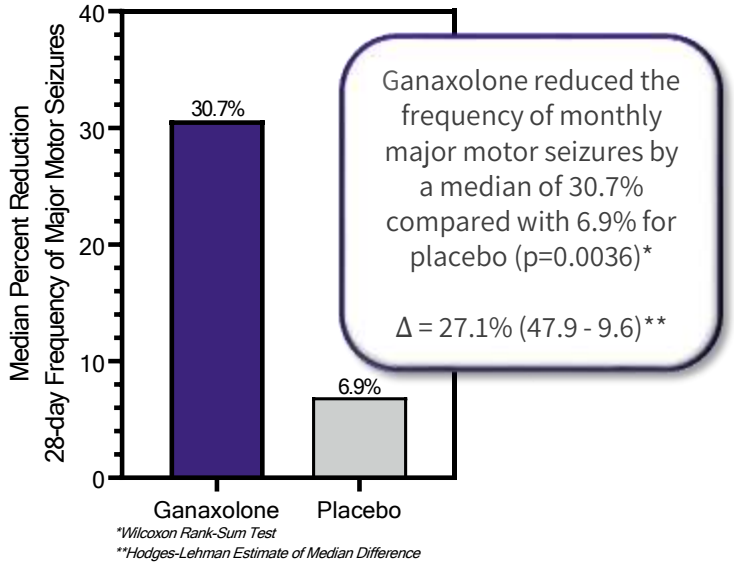
Marigold Study
CDKL5 Deficiency Disorder

Marigold data published in ***The Lancet Neurology***

First international CDKL5 guidelines published in ***Frontiers in Neurology***

OLE data published in ***Epilepsia***

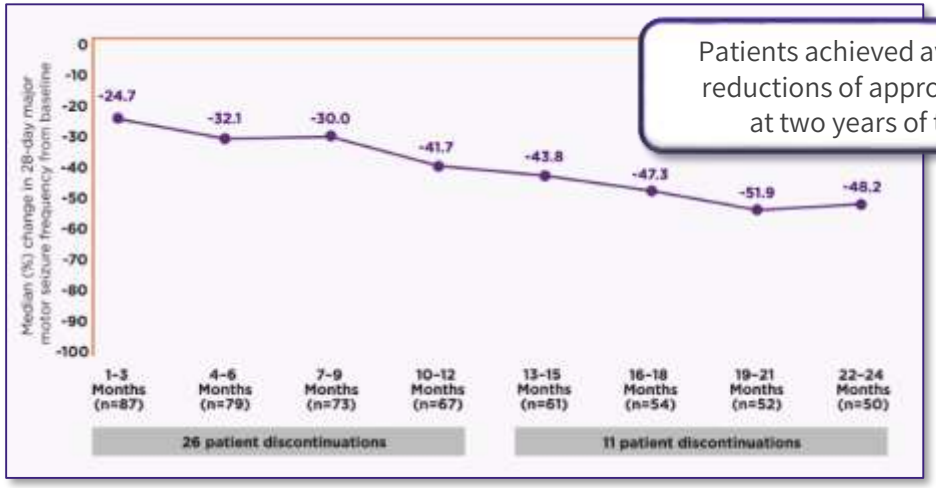
Patients taking ganaxolone experienced a significant reduction in seizure frequency



Ganaxolone reduced the frequency of monthly major motor seizures by a median of 30.7% compared with 6.9% for placebo (p=0.0036)*

Δ = 27.1% (47.9 - 9.6)**

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



Patients achieved average seizure reductions of approximately 50% at two years of treatment

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 ganaxolone- and placebo-treated patients, respectively, during the DB phase.

Patients who remained in the clinical trial at 2 years experienced sustained reduction in MMSF[1]

- 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.

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***Data as of June 30, 2022

1. Data on file. Marinus Pharmaceuticals, Inc.
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.

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ZTALMY® Performance Metrics and Growth Drivers

Net product revenue of **$8.5M for the third quarter** of 2024

56% growth from Q3 2023

Full year 2024 expected net product revenue: **$33M-$34M**

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
- Potential indication expansion
- Ex-U.S. launches

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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 the CDD 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

- Refine the ZTALMYOne™ patient support program to meet the evolving needs of the CDD community

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

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Driving Global Access of ZTALMY® (ganaxolone)

Europe: Collaboration agreement with Orion Corporation for ganaxolone

- Development, commercial and sales milestones[1]; 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

- Development, commercial and sales milestones[2]; tiered double-digit royalties

MENA: Distribution agreement with Biologix Fzco for ganaxolone

- Revenue sharing arrangement with regulatory milestones

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

- Revenue began in Q3 2024 through distribution agreement with Uniphar Group

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[1]Subject to achievement of certain clinical and commercial launch milestones and annualized sales thresholds for the oral and IV products
[2]Subject to achievement of regulatory approvals for CDD

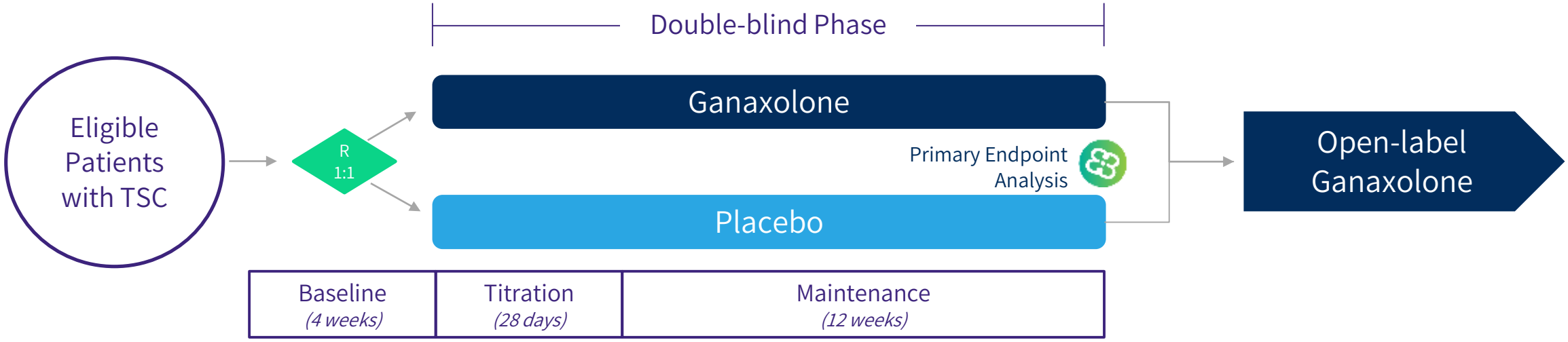
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Phase 3 TrustTSC Topline Trial Results

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Phase 3 Trial Overview



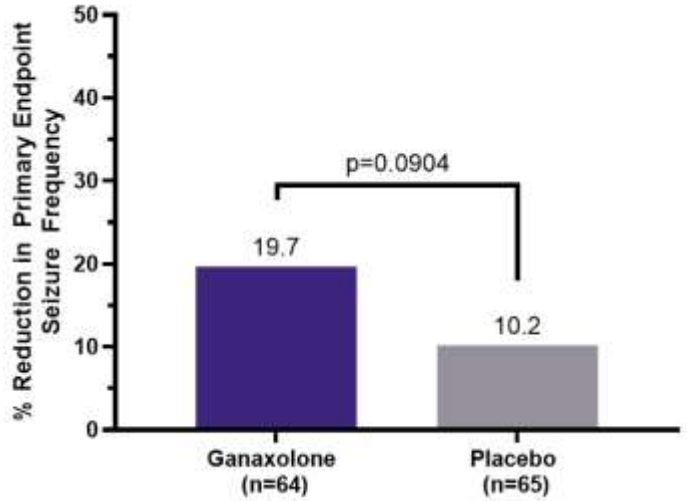
- Enrolled 129 patients across sites in the U.S., Western Europe, Canada, Israel, Australia and China

- **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

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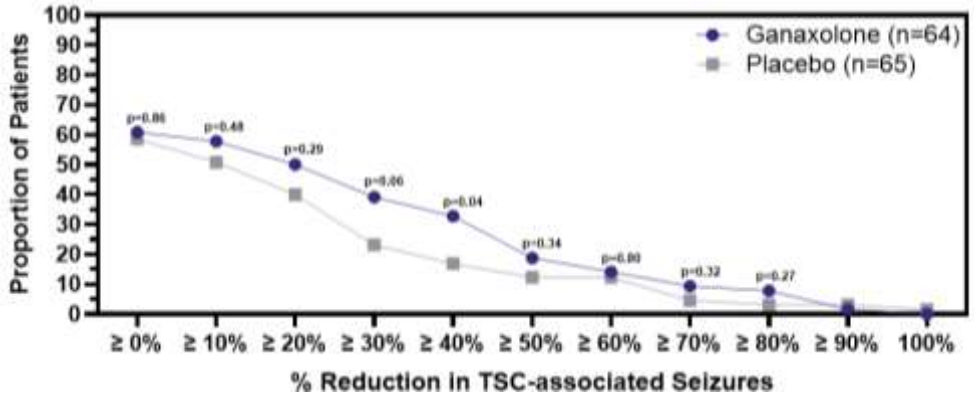
TrustTSC Topline Results

Primary Endpoint

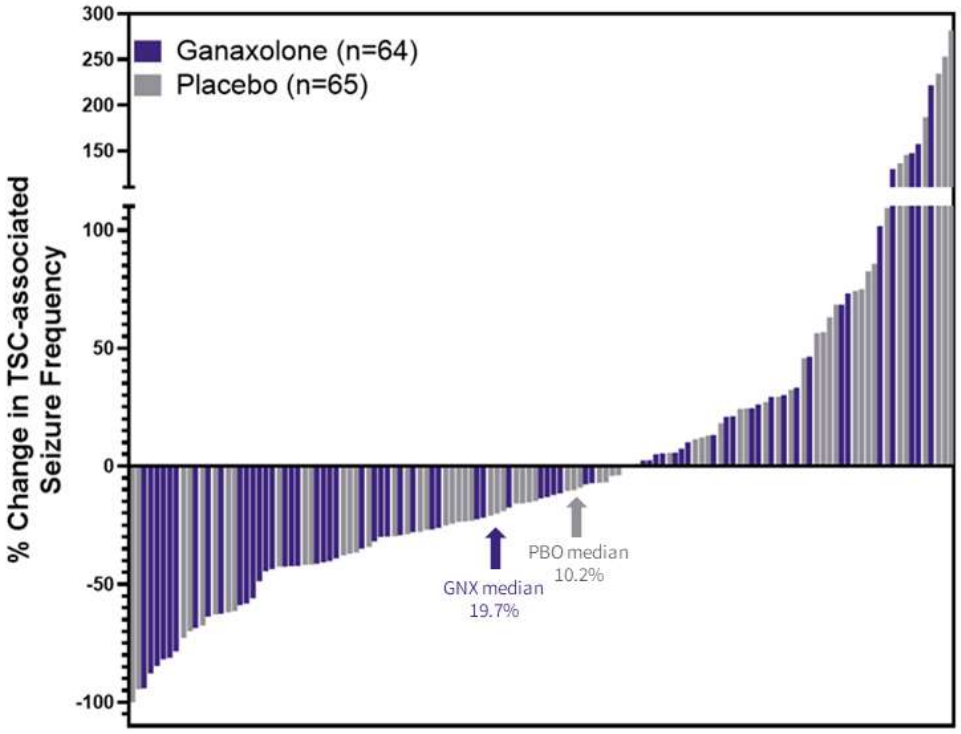


Ganaxolone was generally well-tolerated with a safety profile consistent with previous clinical trials.
The most frequent adverse event was somnolence: 28.1% for ganaxolone compared with 16.9% for placebo.

Responder curve*:



Individual patient outcomes:



*Nominal p-values

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Second Generation Product Development

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Second Generation Ganaxolone - Prodrug

Goals

Increase efficacy
Consistent delivery to achieve target plasma concentration

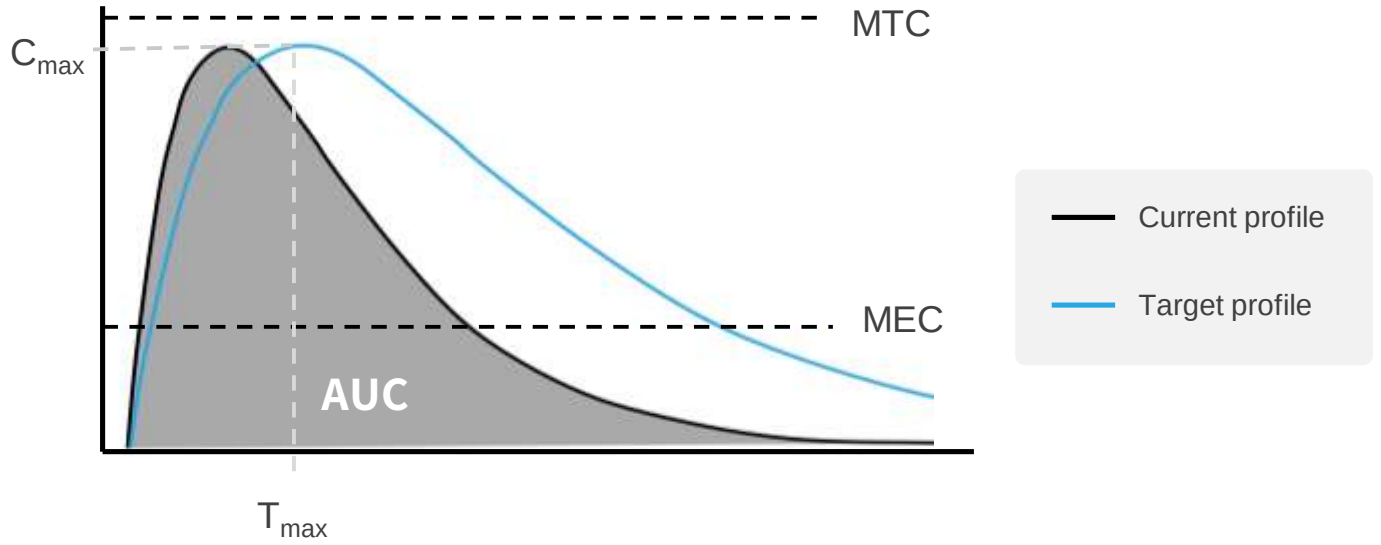
Improve tolerability
Optimize PK profile to reduce Cmax-related adverse effects

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 candidate identified
- IND-enabling work estimated to take 12-15 months to complete
- IP filed in 2022

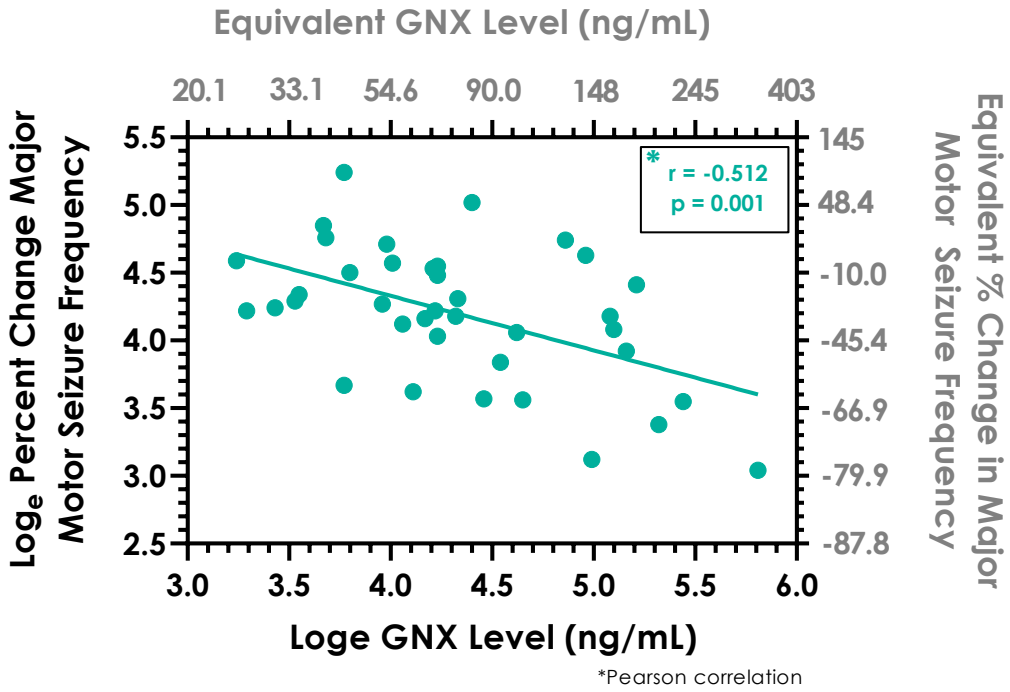
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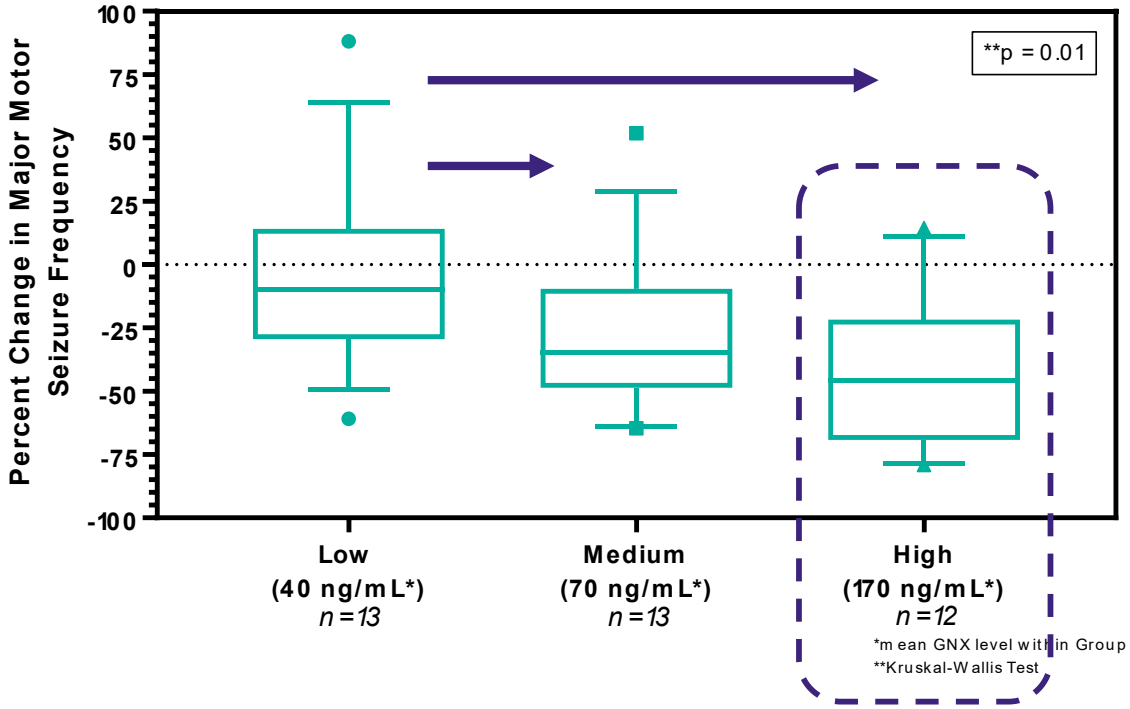
Average Ganaxolone Levels Correlate with Seizure Reduction

Marigold Study
CDKL5 Deficiency Disorder

- 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 ganaxolone dose level groups



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



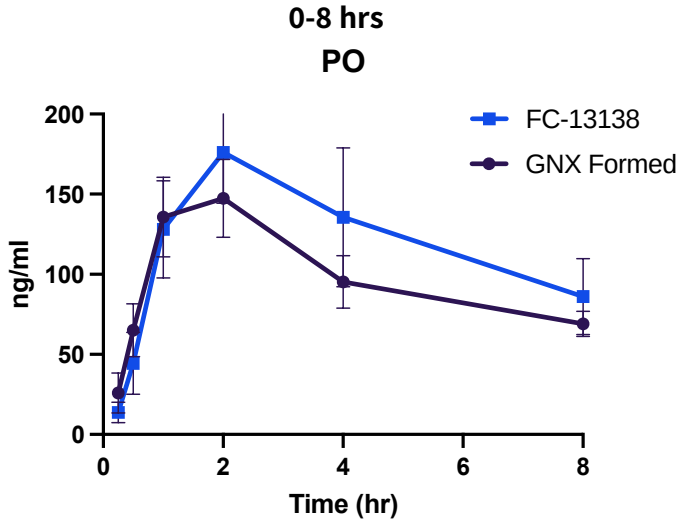
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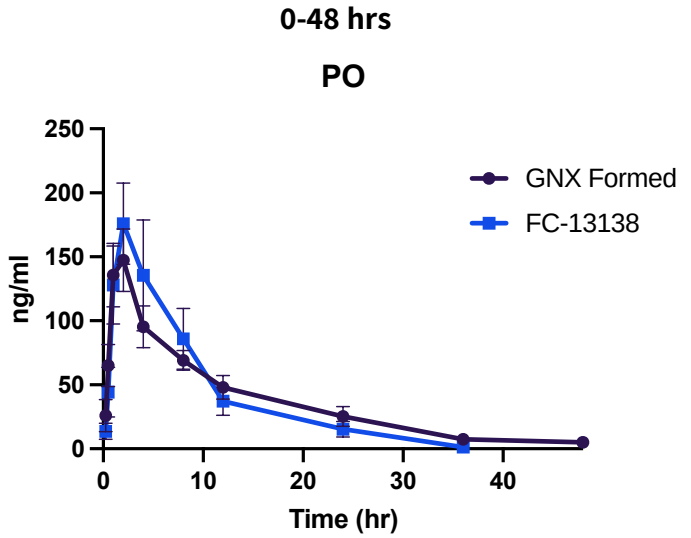
Loge percentage change in major motor seizure frequency was calculated as loge(percentage change + 100)

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Ganaxolone Prodrug Program Overview

- Ganaxolone prodrug IND readiness requires 12-15 month investment; near-term investment in analytical chemistry development work
- Prodrug compound readily converts to ganaxolone *in vivo* in dog following single oral administration (figures on right)
- Preferred synthesis route ready for non-GMP tox scale-up
- Salt screening nearly complete and shows ideal profile at low pH for improved solubility for oral administration
- Early PK work supports QD or BID dosing and the ability to achieve higher steady state serum concentrations.





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Phase 3 RAISE Topline Trial Results

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Status Epilepticus Overview

Status Epilepticus =

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 t_1)*
- *can have long-term consequences (after time point t_2)*



Incidence of SE in the United States:

~150,000

SE episodes per year[1]



Associated with significant morbidity:

- **Disabling cognitive deficits[2]**
- **Increased risk for development of epilepsy[2]**



Increased mortality associated with:

- **Underlying SE etiology[3]**
- **More refractory SE[4]**
- **Therapeutic coma exposure[3]**
- **Increased age[3]**



Significant healthcare utilization:

- **Substantial direct healthcare cost[5] especially as SE progresses[6]**

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1. DeLorenzo RJ *et* al 1995 J Clin Neurophysiol 2. Naylor DE. Epilepsia Open. 2023
3. Rossetti AO, et al. J Neurol Neurosurg Psychiatry. 2006 4. Jayalakshmi S, et al. Seizure. 2015
5. Penberthy LT, et al. Seizure. 2005 6. Guterman EL, et al. JAMA Neurol 2021

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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*



INTERVENTION

1:1 randomization

- **Background Standard of Care + IV Ganaxolone**
- **Background Standard of Care + Placebo**

CO-PRIMARY ENDPOINTS

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

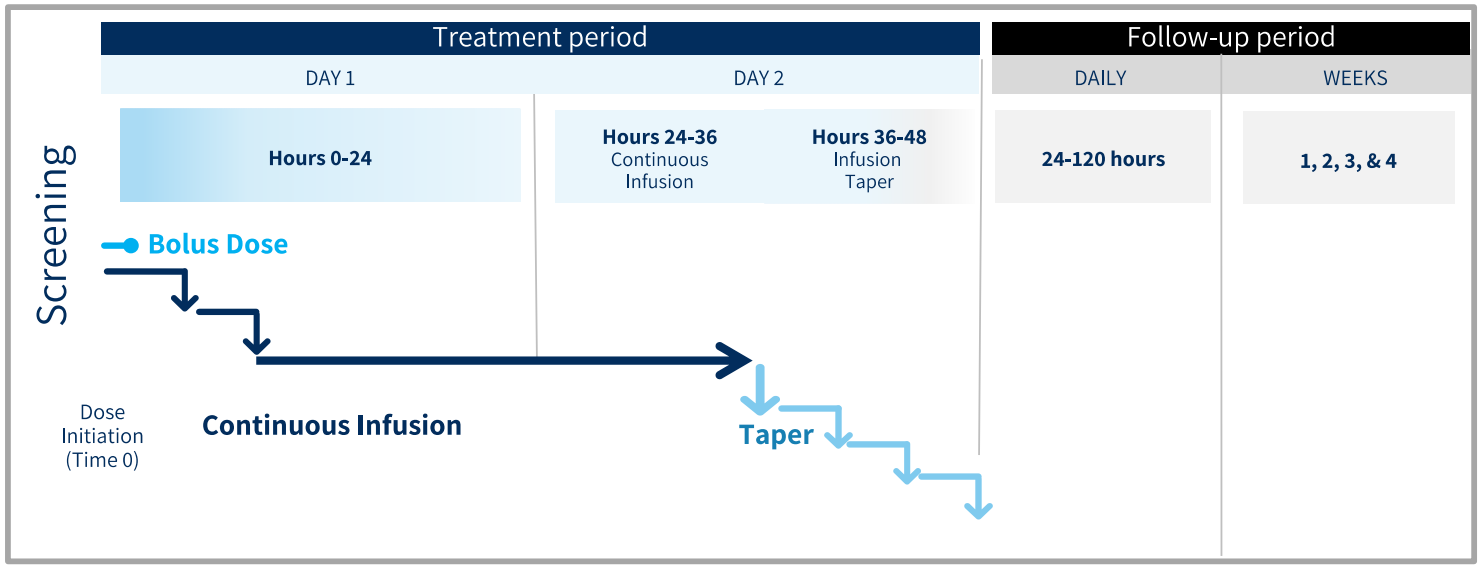
Durability of Effect: Proportion of patients with **no progression to IV anesthesia for 36 hours**

KEY SECONDARY ENDPOINTS

Onset of Action: Time to SE cessation

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

DOSING REGIMEN



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RAISE Topline Results: Baseline Patient 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)	3 (1, 4)	3 (2, 5)
Score 0-2, no. % (Favorable)	22 (44.9)	14 (27.5)
Score 3-6, no. % (Unfavorable)	25 (51.0)	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)

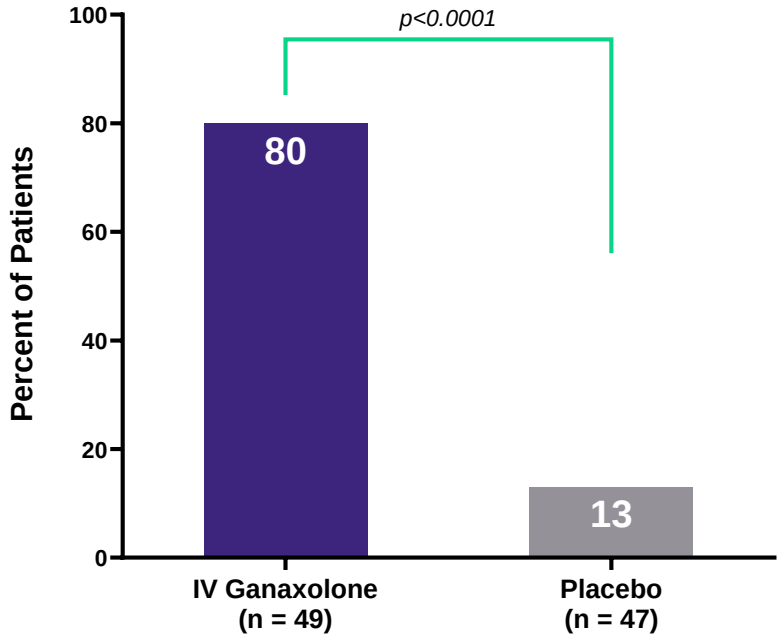
Demographic data indicate imbalance in several baseline characteristics

*Safety population (unless otherwise noted)
[A]ITT population

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RAISE Topline Results: Co-Primary Endpoints

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

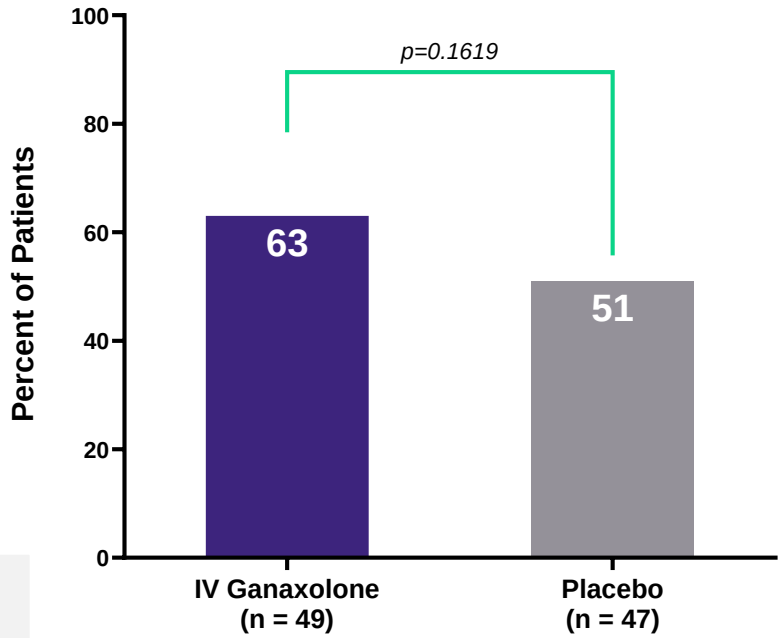


Median time to SE Cessation*:

IV ganaxolone: 4.2 minutes
Placebo: 307.2 minutes

nominal p<0.0001

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



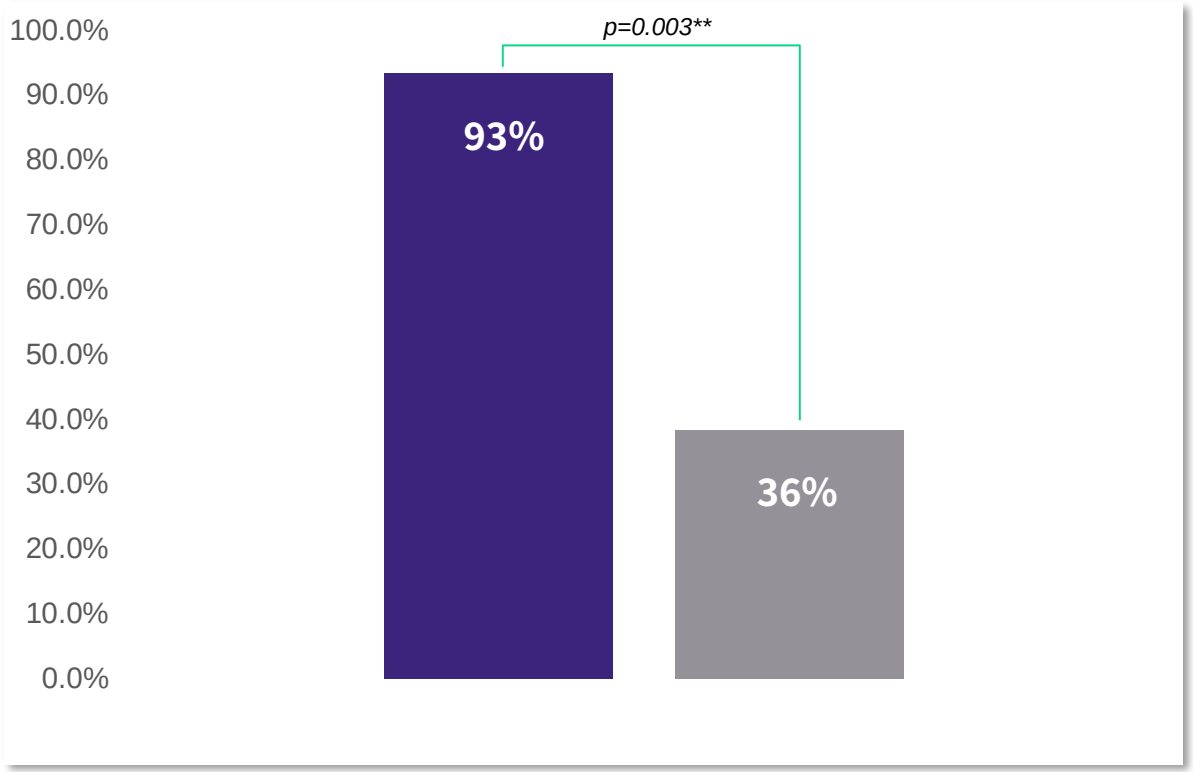
The incidence of serious adverse events was similar between the treatment and placebo arms (n=19 for IV ganaxolone, n=18 for placebo), with hypotension being more commonly seen in the IV ganaxolone arm.

*Time to SE cessation after study drug administration on top of background standard of care, investigators could choose to escalate background standard of care treatment at any point to manage patient care.

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RAISE Topline Results: EEG Secondary Endpoint

Median percent reduction in EEG seizure burden - hours 1-36*



*Data reported is the pre-anesthesia seizure burden, with EEG seizure burden after the initiation of IV anesthesia imputed as the mean hourly seizure burden from the start of the study drug up to the hour prior to IV anesthesia

**Nominal p-value

EEG seizure burden is a potential measure of durability of effect

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Financial Update

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Financial Overview

2024 Full Year Guidance

Guidance

	Full Year 2024
ZTALMY Net Revenue	$33 - $34 million
SG&A & R&D[1]	$135 - $138 million
SBC[2]	~$20 million

Financial Summary (at Sept. 30, 2024):

- $42.2 million in cash and cash equivalents
- Cash runway into Q2 2025
- 55.2 million shares outstanding; 67.9 million shares outstanding on a fully dilutive basis[3]
- $56.2 million of outstanding debt, matures May 2026

Nasdaq: MRNS

Analyst Coverage*:

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

EF Hutton: Jason Kolbert

H.C. Wainwright & Co: Douglas Tsao

Jefferies: Andrew Tsai

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

Leerink Partners: Marc Goodman

RBC: Brian Abrahams, M.D.

RW Baird: Brian Skorney

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

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

[1] Reflects 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.

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Intellectual Property



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Multiple Layers Of Potential Protection

U.S. Patents/ Patent Applications		Expiration Date
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)
Epilepsy		
Method of Use	Patent granted on oral titration regimen	2042
	Applications pending on oral titration regimens	2042
Formulation	Patents granted (oral suspension)	2031 (if PTE granted)
Second Generation Ganaxolone		
Prodrug	Application pending on ganaxolone prodrug	2042/2043
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
	Applications pending on IV formulation	2036

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Orphan drug designations for CDD and PCDH19 provide 7 and 10 years regulatory exclusivity in U.S. and EU, respectively.
Orphan drug designation for SE provides 7 years regulatory exclusivity in U.S.

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