Corporate Presentation

July 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 trial 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.

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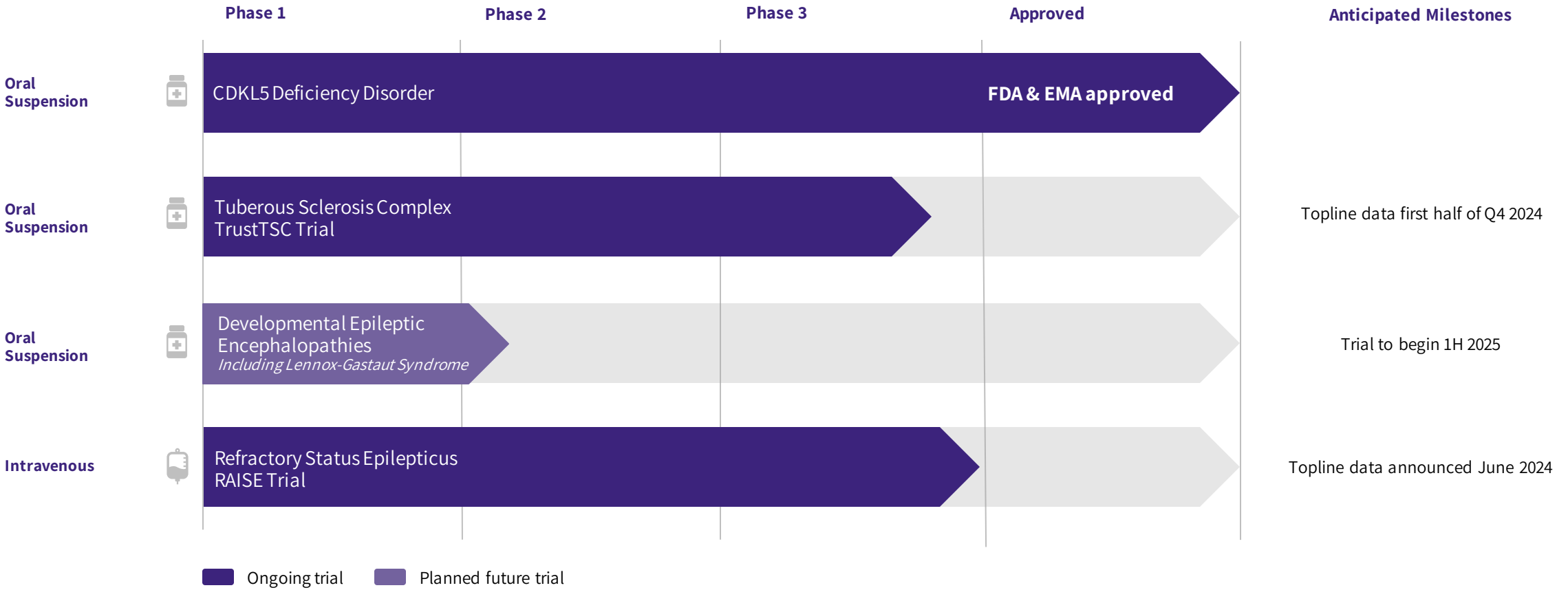
Ganaxolone Development Pipeline



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.



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ZTALMY® Clinical and Commercial Overview

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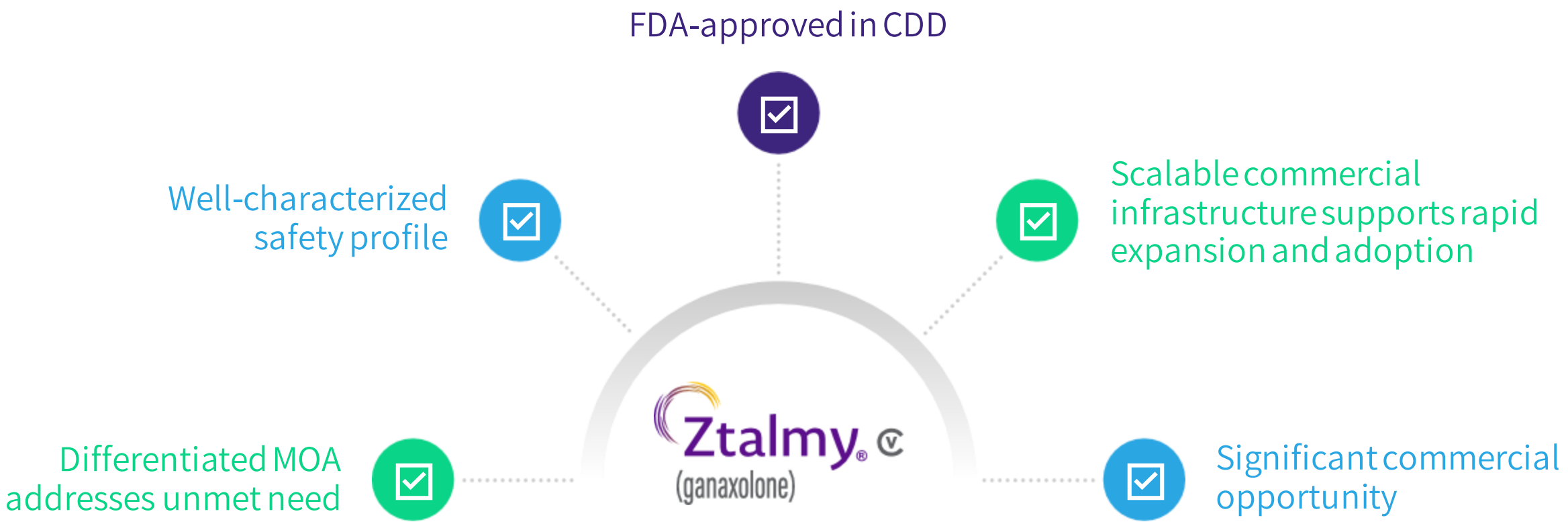
ZTALMY® Has the Potential to Significantly Advance Epilepsy Treatment



CDD: CDKL5 deficiency disorder; MOA: mechanism of action

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Phase 3 CDD Marigold Trial Data and Safety Summary

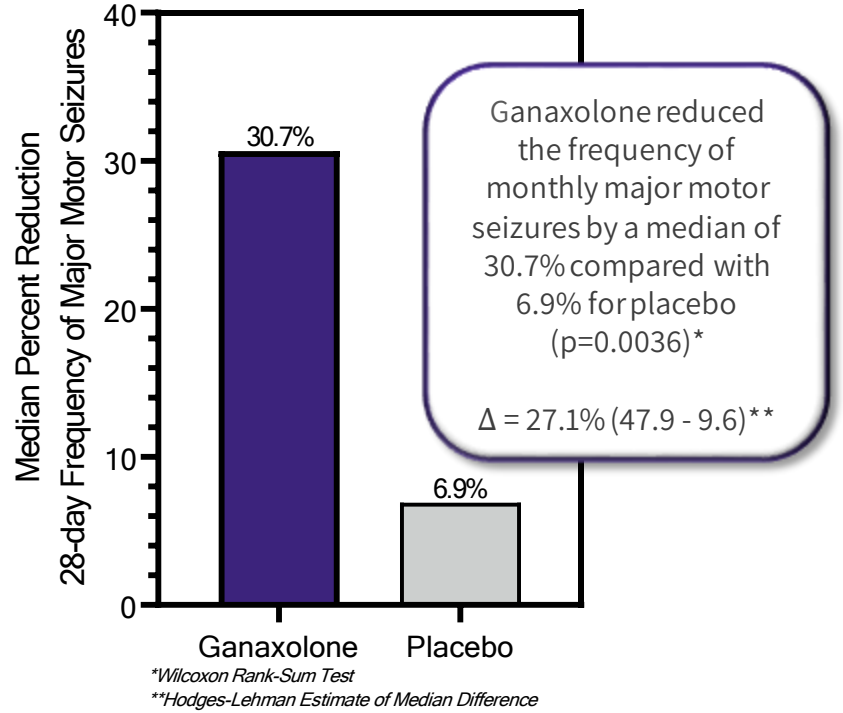
Marigold Study
CDKL5 Deficiency Disorder

Phase 3 Marigold data published in ***The Lancet Neurology***

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



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)**

*Hodges-Lehmann estimate of median difference (95% confidence interval)
**Wilcoxon rank-sum test

Treatment Emergent Adverse Events (TEAE)

Preferred Term	Placebo (n=51)	Ganaxolone (n=50)
Any TEAE, n (%)	45 (88.2)	43 (86.0)
Somnolence	8 (15.7)	18 (36.0)
Pyrexia	4 (7.8)	9 (18.0)
Upper Respiratory Tract Infection	3 (5.9)	5 (10.0)
Constipation	3 (5.9)	3 (6.0)
Salivary Hypersecretion	1 (2.0)	3 (6.0)
Sedation	2 (3.9)	3 (6.0)

Serious Treatment Emergent Adverse Events

Preferred Term	Placebo (n=51)	Ganaxolone (n=50)
Any Serious TEAE, n (%)	5 (9.8)	6 (12.0)
Bronchitis	0 (0.0)	1 (2.0)
Rhinovirus Infection	0 (0.0)	1 (2.0)
Urinary Tract Infection	0 (0.0)	1 (2.0)
Pneumonia Mycoplasmal	1 (2.0)	0 (0.0)
Pneumonia Viral	1 (2.0)	0 (0.0)
Respiratory Syncytial Virus Bronchiolitis	1 (2.0)	0 (0.0)
Oxygen Saturation Decreased	0 (0.0)	1 (2.0)
Food Refusal	0 (0.0)	1 (2.0)
Pneumonia Aspiration	0 (0.0)	1 (2.0)
Hypoxia	1 (2.0)	0 (0.0)
Faecaloma	1 (2.0)	0 (0.0)
Hypotonia	1 (2.0)	0 (0.0)
Seizure	1 (2.0)	0 (0.0)
Unresponsive to Stimuli	1 (2.0)	0 (0.0)

Includes AEs that occurred >5% of subjects in ganaxolone arm and ganaxolone > placebo

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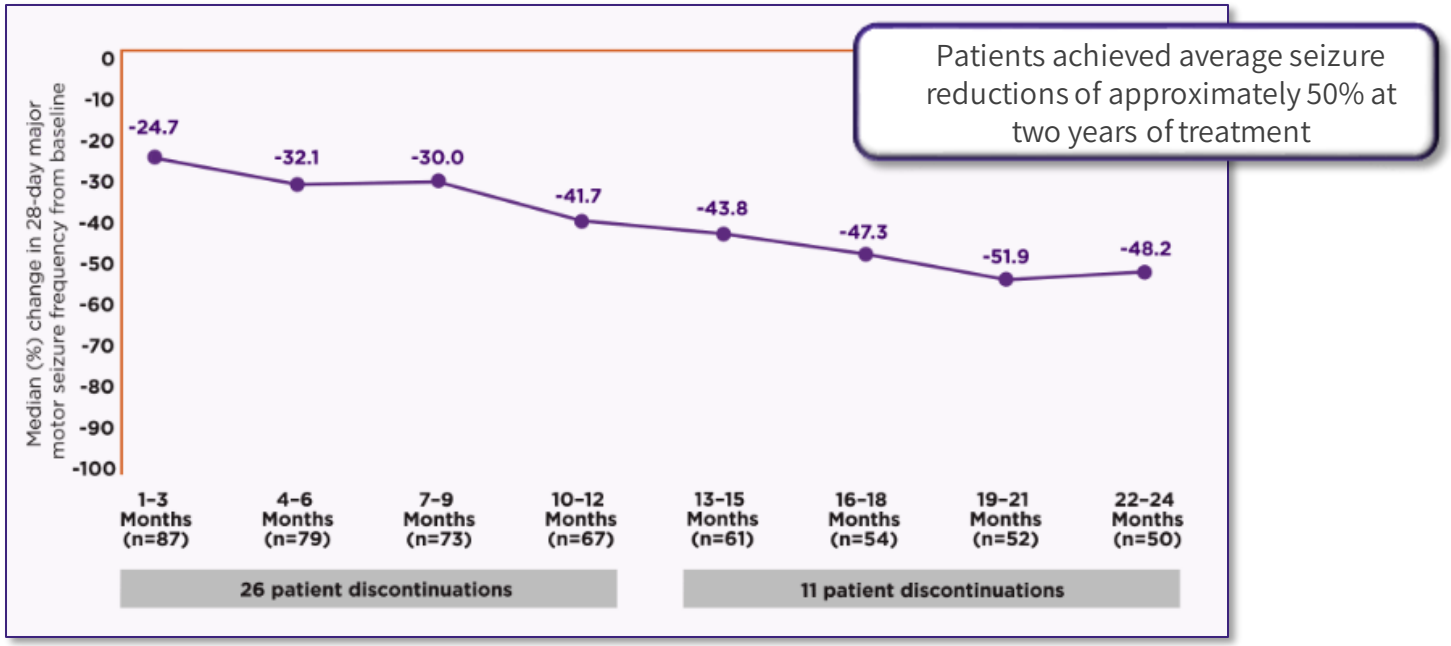
Phase 3 Open Label Extension Data in CDD

Marigold Study
CDKL5 Deficiency Disorder

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

Trial data published in *Epilepsia*



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.

*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

U.S. net product revenue of **$7.5M for the first quarter** of 2024

>125% growth from Q1 2023

Increased full year 2024 expected U.S. net product revenue to **$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)

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Significant Near-term Milestones Build on Commercial Success

Program	Indication	1H 2024	2H 2024	1H 2025	2H 2025
Ztalmy® (ganaxolone)	CDKL5 deficiency disorder	☑ **Achieved profitability***			
	Tuberous sclerosis complex	☑ **Completed Phase 3 enrollment**	Phase 3 TrustTSC readout	Potential filing for FDA Approval	Potential Launch
	Developmental and epileptic encephalopathies			Begin enrollment of Phase 2 trial	
Second-Gen Program	Lennox-Gastaut syndrome				IND Expected

Topline Data Readout Expected Before Year-End

MARINUS *on ZTALMY commercial investment

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Driving Global Access of ZTALMY® (ganaxolone)

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

- Up to €90 million of 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 in CDD, TSC, SE

- Up to $256 million of 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

Program initiated in Q4 2023 to expand global access to ZTALMY in non-partnered markets for appropriate patients with seizures associated with CDD

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

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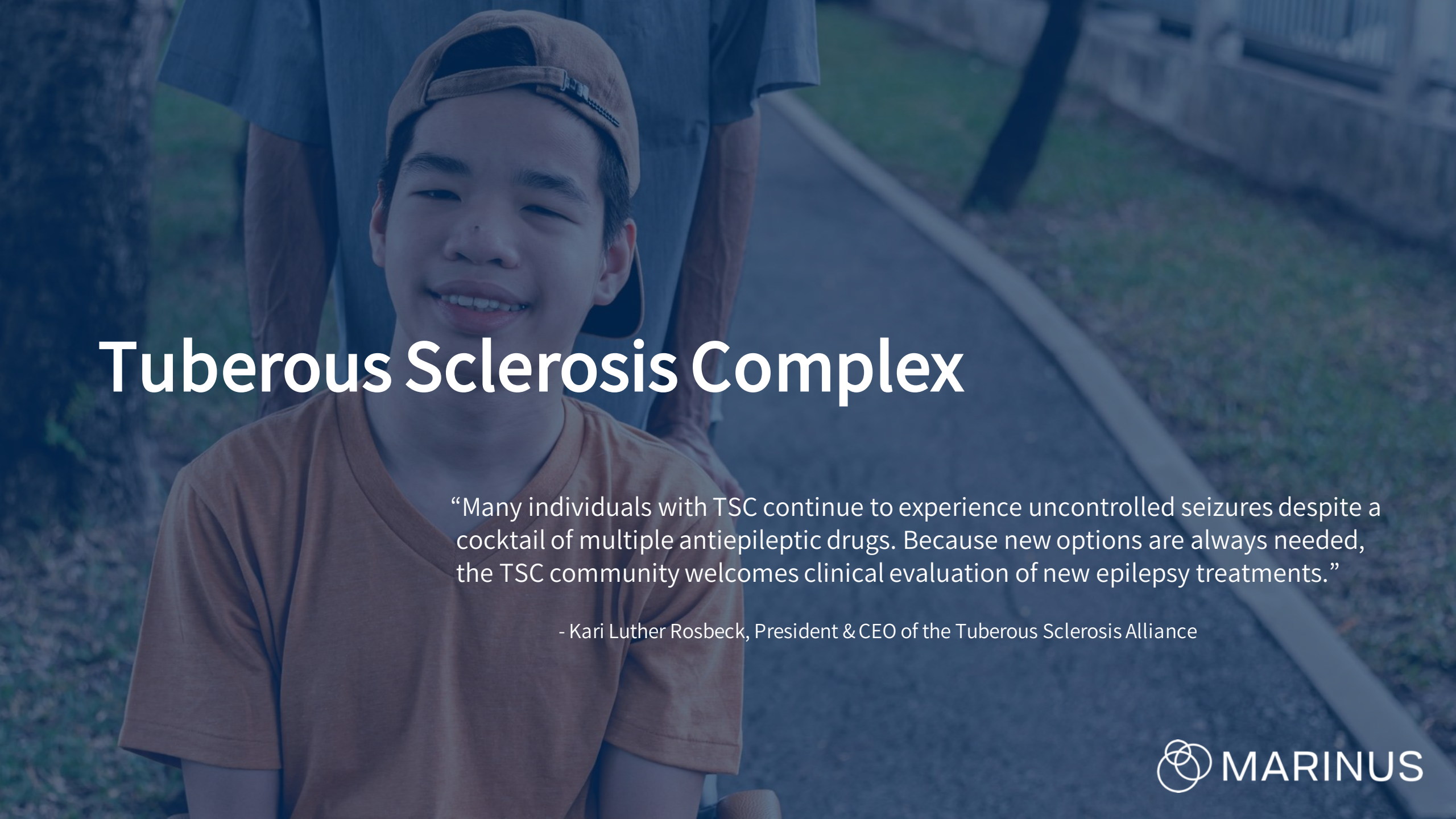

Tuberous Sclerosis Complex

"Many individuals with TSC continue to experience uncontrolled seizures despite a cocktail of multiple antiepileptic drugs. Because new options are always needed, the TSC community welcomes clinical evaluation of new epilepsy treatments."

- Kari Luther Rosbeck, President & CEO of the Tuberous Sclerosis Alliance

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Tuberous Sclerosis Complex (TSC)

CAUSE	• Defect or mutation of *TSC1* and/or *TSC2* genes
INCIDENCE	• ~1 in 6,000 live births[1]
COMMON SYMPTOMS	• Seizures, cognitive impairment, behavioral difficulties, skin/kidney/lung abnormalities, etc.
EPILEPSY IN TSC	• Occurs in ~80-90% of those with TSC[2] • 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

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1. Hasbani DM & Crino PB 2018 Hand. Clin. Neurol.
2. Chu-Shore CJ *et al.* 2010 Epilepsia

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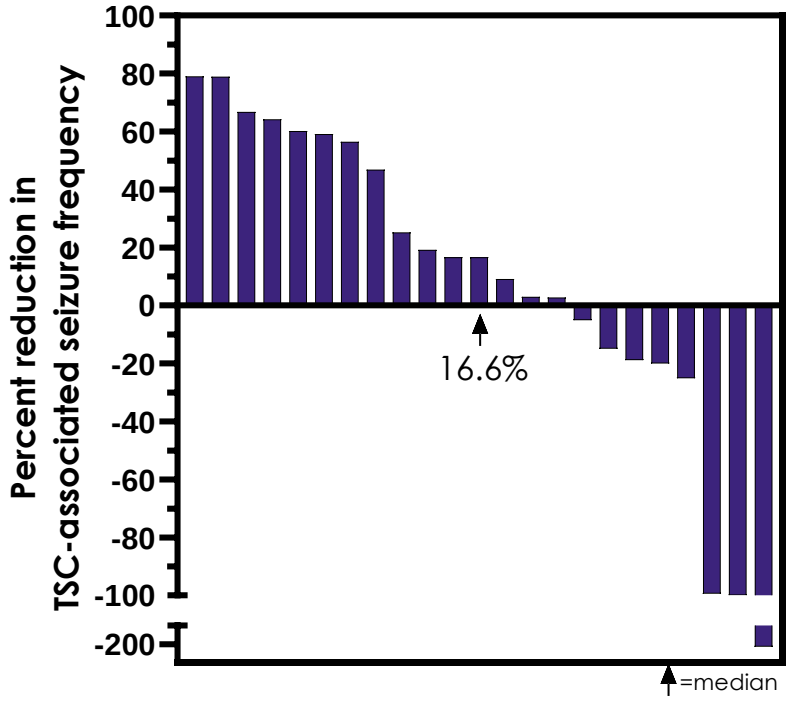
TSC Phase 2 Trial Results

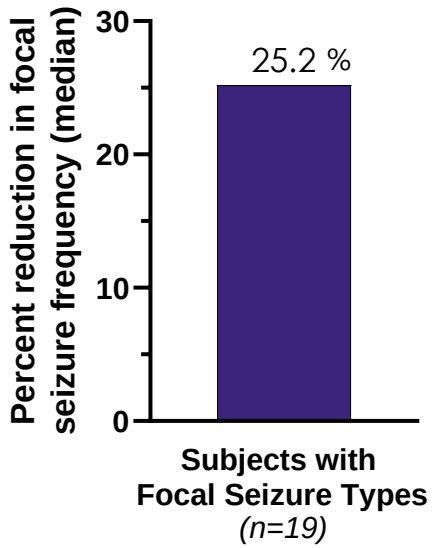
CALM STUDY

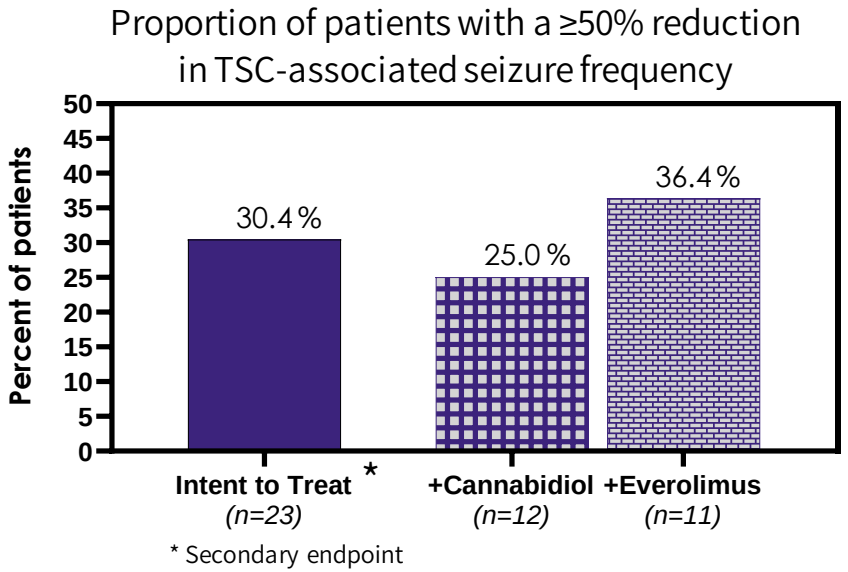
Primary Endpoint Results:

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

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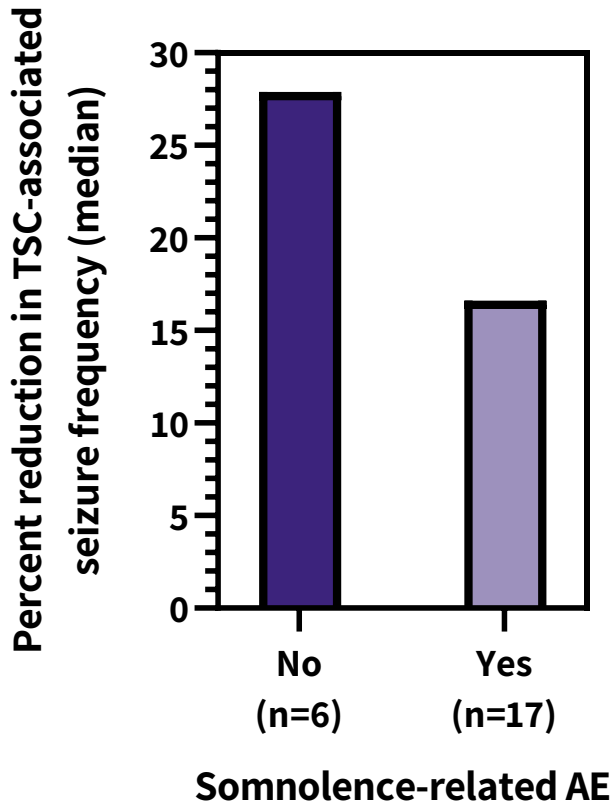
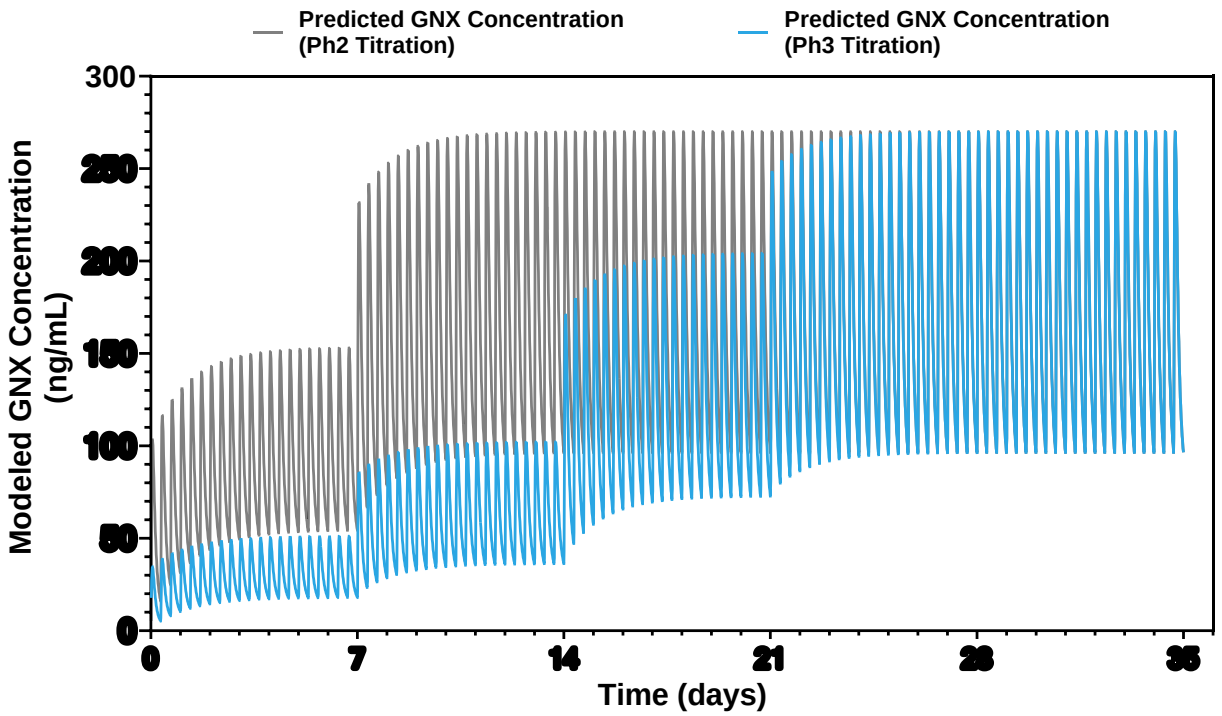
Phase 3 Protocol Refinements Informed by Phase 2 Tolerability

Phase 2
Patients without somnolence related AEs experienced greater seizure reductions



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



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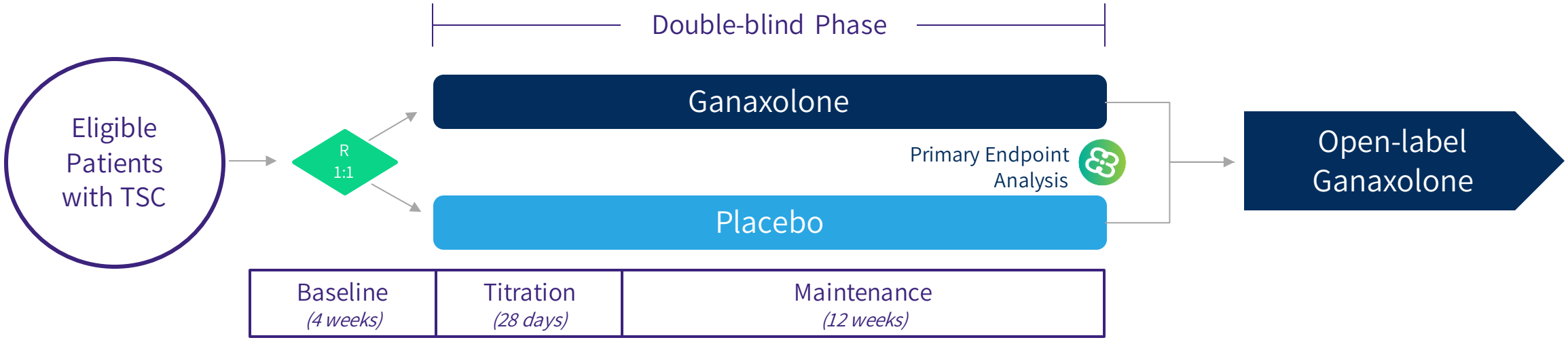
Phase 3 Trial Overview



- 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 priority review expected

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TrustTSC Baseline Demographics*

Failed Therapies*
(mean)

4.8

Epidiolex®/ CBD	mTor inhibitors (everolimus, sirolimus, tacrolimus)
27%	58%

Age
(mean [min-max])

15 [1-50]

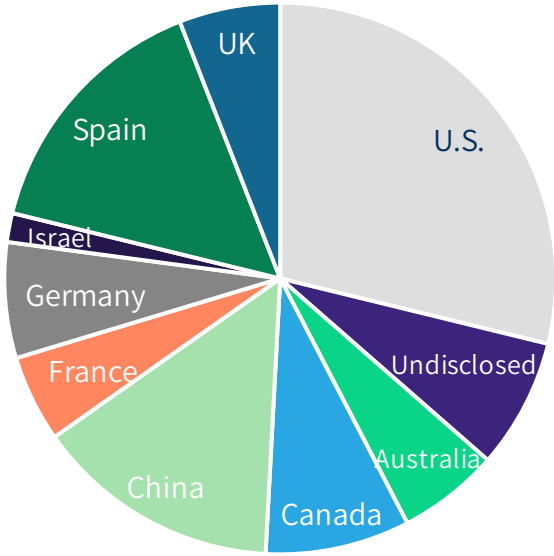
Gender

52%	48%
male	female

Baseline Seizure Rate
(median, per 28 days)

50

Recruitment by Country



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

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

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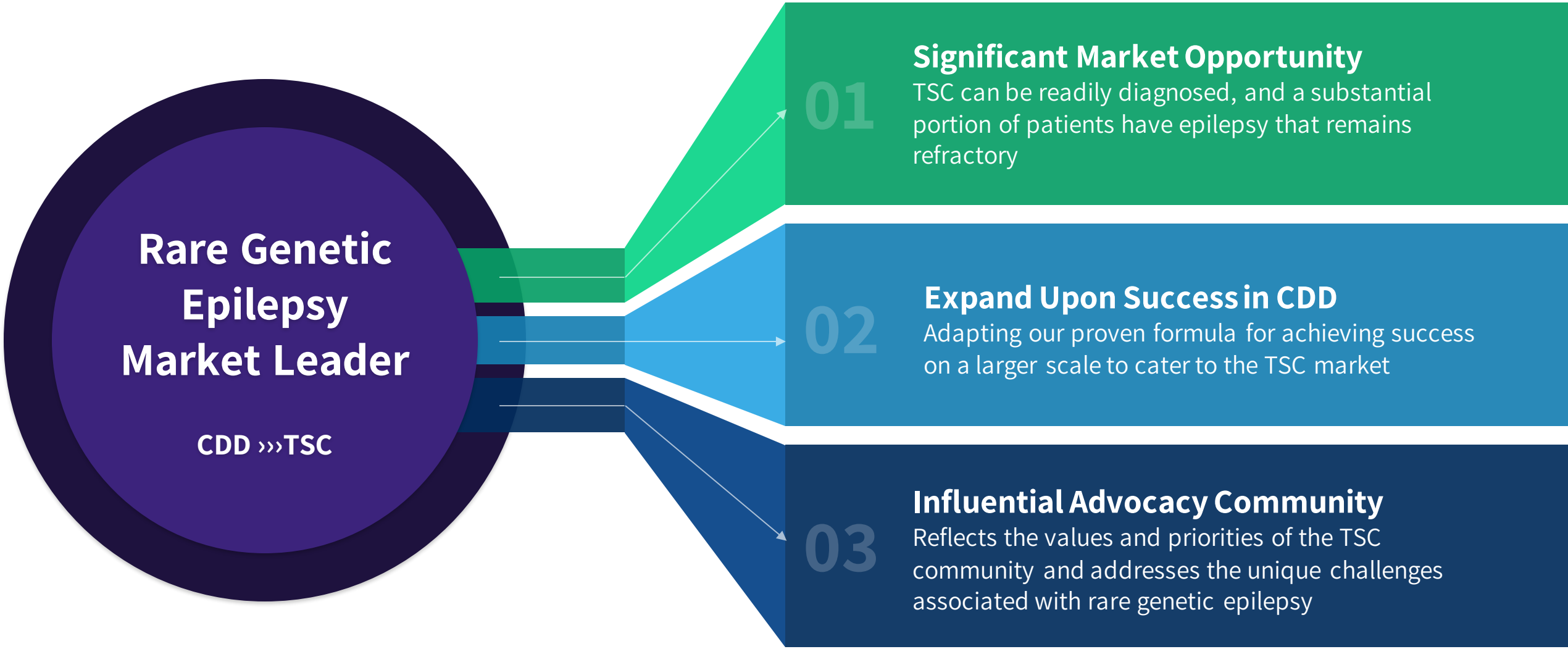
Anticipated Commercial Expansion into Tuberous Sclerosis Complex



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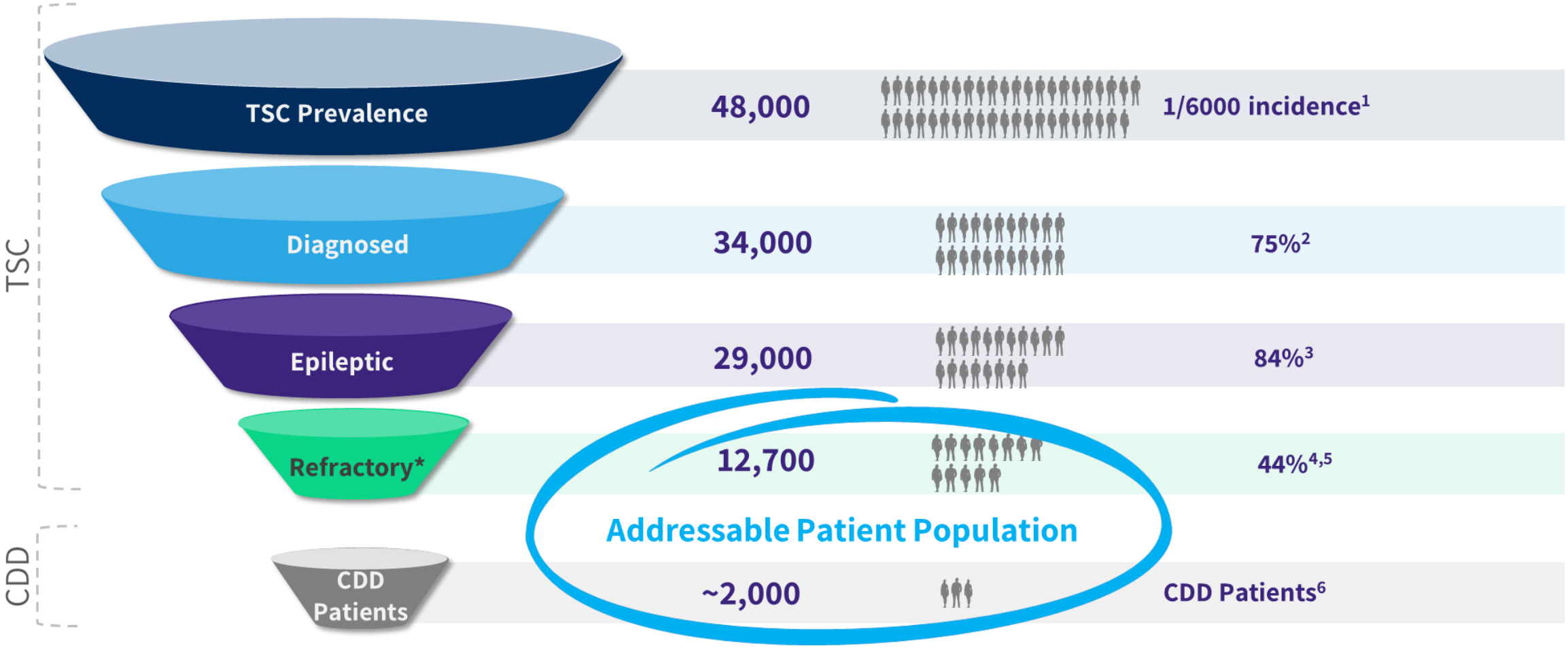
Unlocking a 4-5x Growth Opportunity for ZTALMY® in TSC



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

[1]TSC Alliance; [2]Marinus ZS Opportunity Assessment, 2020 Market Research; [3]Curatolo P - Epilepsy in TSC: Findings from the TOSCA Study;
[4]Chu-Shore CJ et al.The natural history of epilepsy in tuberous sclerosis complex. Epilepsia.; [5]63% (Chu-Shore) adjust -19% for Epidiolex & Afinitor Utilization 2010;
[6]Estimated 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

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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

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

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

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

STRONG ADVOCACY PARTNERSHIPS
- Community and caregiver education
- Caregiver activation

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

Existing ZTALMY CDD Commercial Organization

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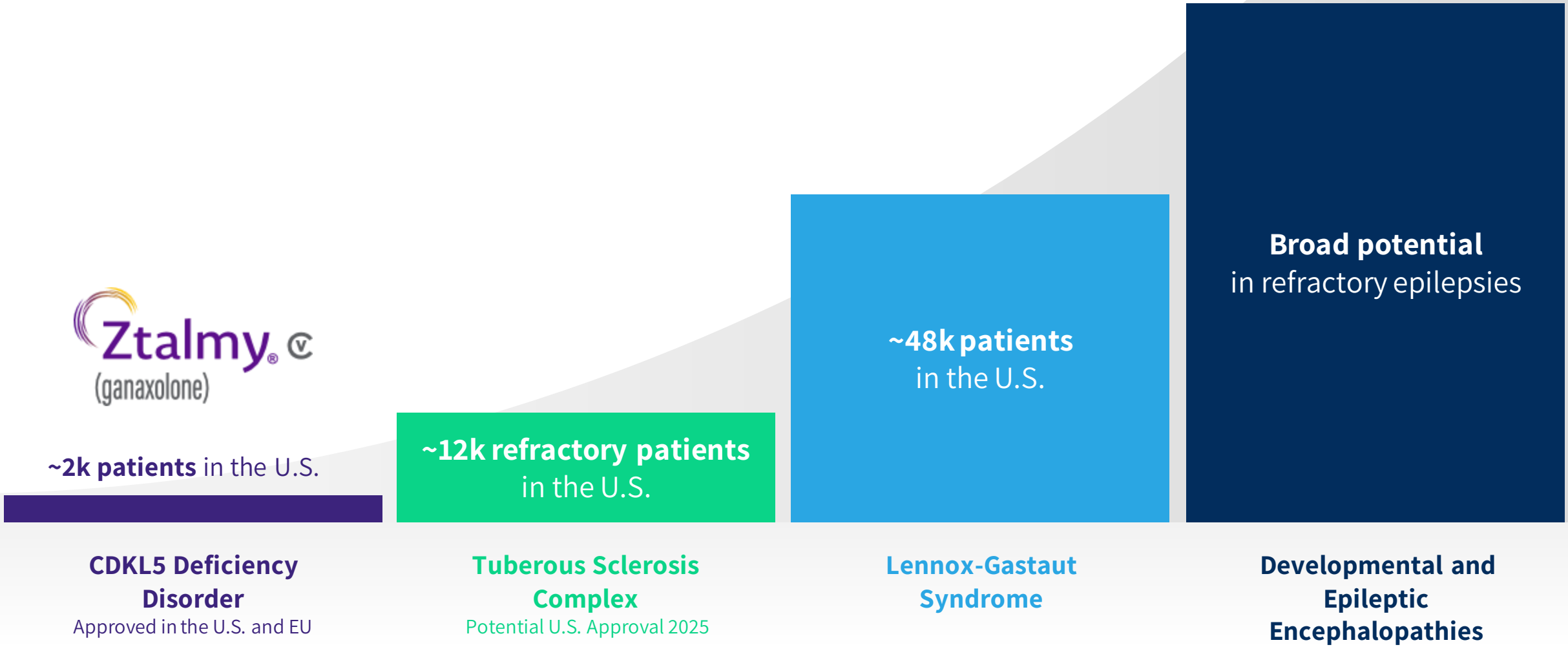
Significant Growth Potential with Expansion into Larger Indications



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Second Generation Product Development

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Second Generation Ganaxolone

Goals

Increase efficacy
Consistent delivery to achieve target plasma concentration

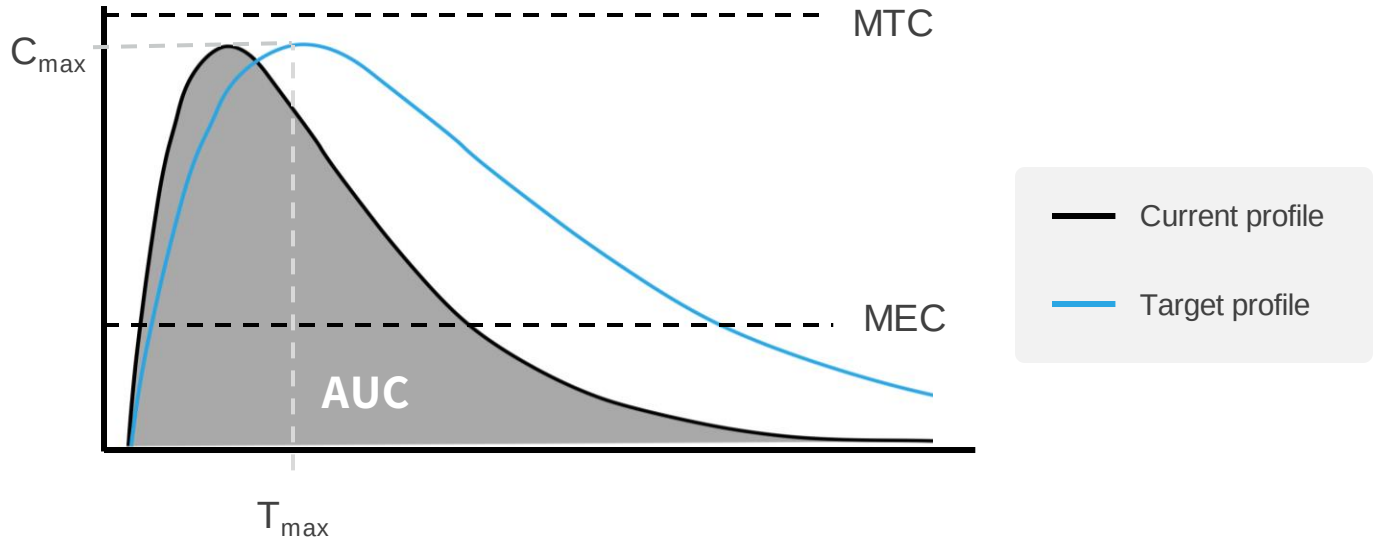
Improve tolerability
Optimize PK profile to reduce Cmax-related adverse effects

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)

Second-generation ganaxolone development approaches:
- Reformulation
- Prodrug

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Next Steps: Prodrug and Ganaxolone Reformulation

Ganaxolone Prodrug

Oral prodrug candidate selected

Goals:
- Optimize PK parameters for efficacy, tolerability and dosing frequency
- Increase absorption (oral), solubility (IV)

Preclinical IND-enabling trials planned

Clinical: IND to follow completion of planned preclinical studies

Second generation ganaxolone formulation goals

- Linear kinetics
- Achieve steady state 100-200 ng/mL
- Minimize peak-trough variability
- Allow once or twice daily dosing while maintaining adequate trough level at steady state (Average trough levels in Marigold study were ~88 ng/mL)

Phase 1 multiple ascending dose (MAD) study of a second generation ganaxolone formulation:

- Preliminary results demonstrated linear kinetics through a wide dose range that could allow individualization of treatment in patients with refractory epilepsy
- Expect to apply extended-release technologies to the formulation targeting consistent exposure to achieve once or twice daily dosing while allowing physicians to dose titrate to higher serum concentrations of ganaxolone

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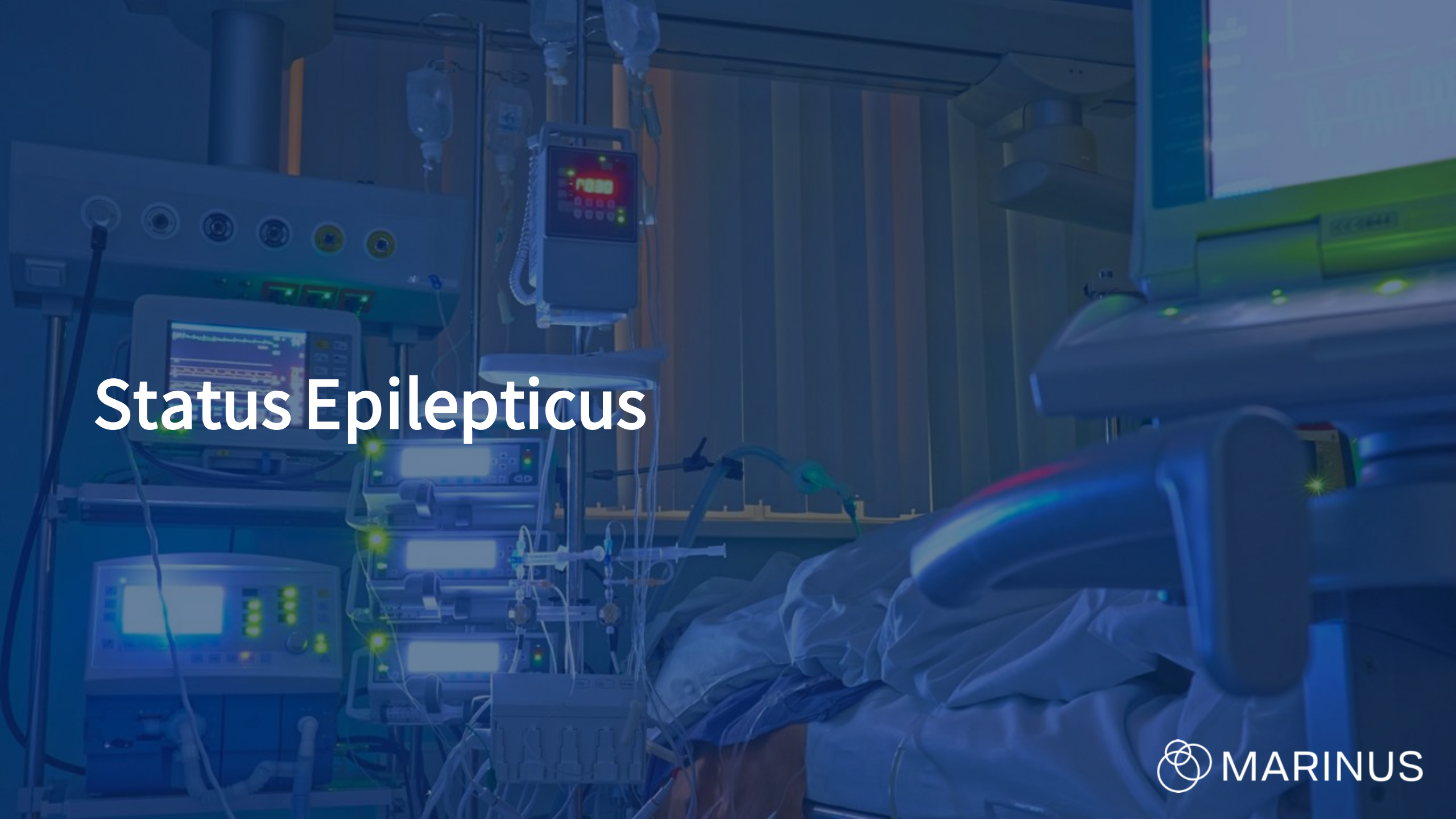

Status Epilepticus

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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 in survivors:

- **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]**

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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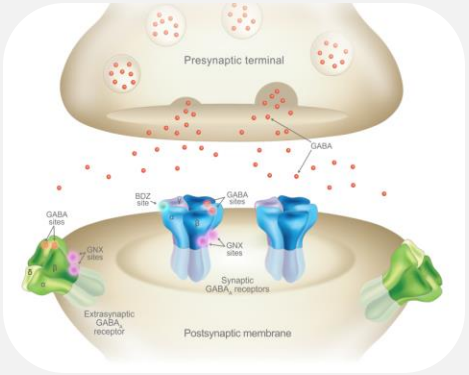
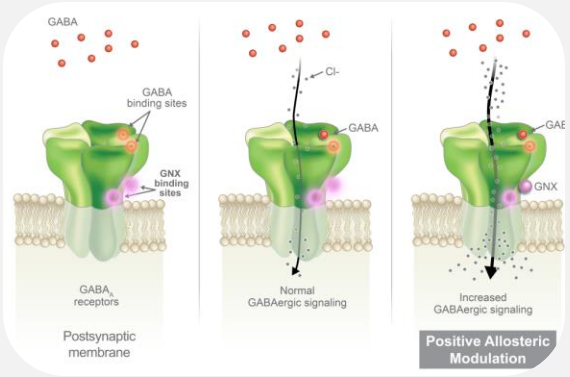
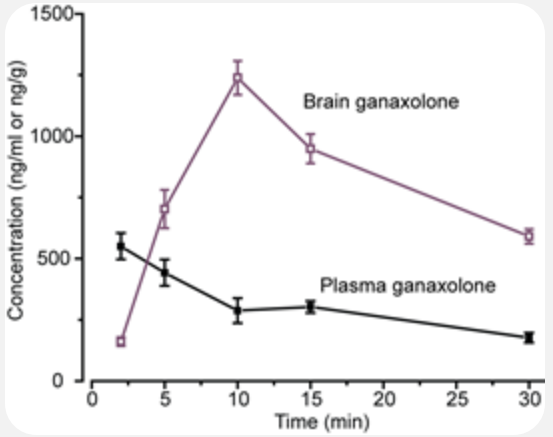
Pharmacokinetics/Pharmacodynamics Well Suited for Acute SE Treatment

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





Experimental PK – plasma and brain[1]



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

Human PK[2]

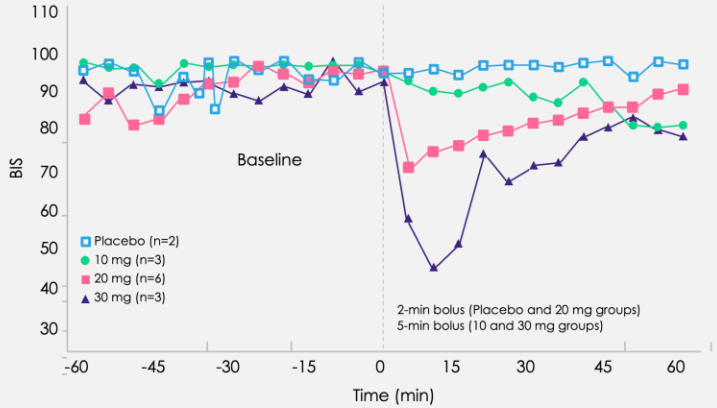
Following 30 mg ganaxolone bolus (over 5 minutes):

C_{max} 1,240 ng/mL

T_{max} 0.08 hrs

Human PD – EEG changes[2]

EEG bispectral index in healthy volunteers following IV ganaxolone



1. 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.
2. Data on file, Marinus Pharmaceuticals, inc.

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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**

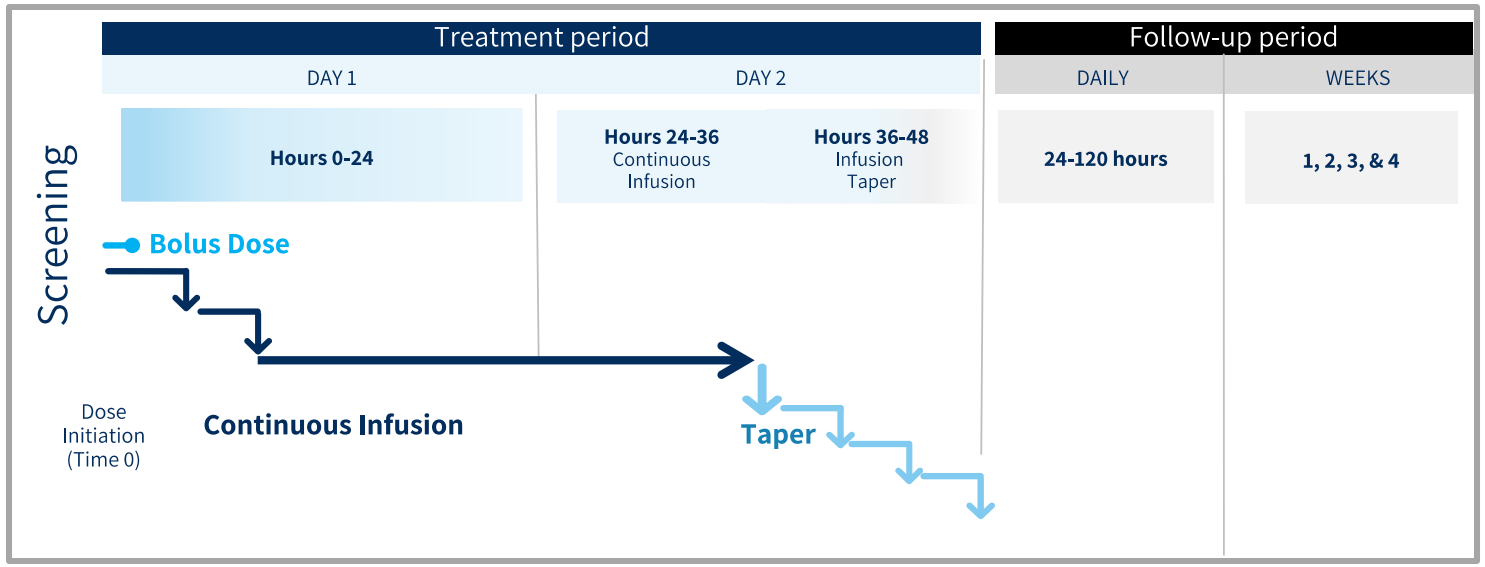
Durability of Effect: Proportion of patients with **no progression to IV anesthesia for 36 hours**

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: 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)	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)	3.2 (1.7)
Seizure burden (%), mean (SD)	29 (29)	24 (23)
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)
[A]ITT population

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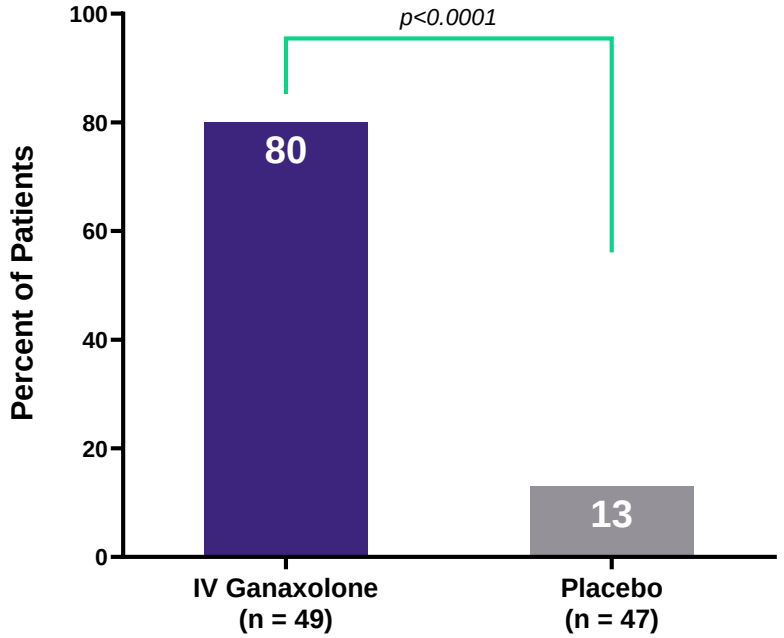
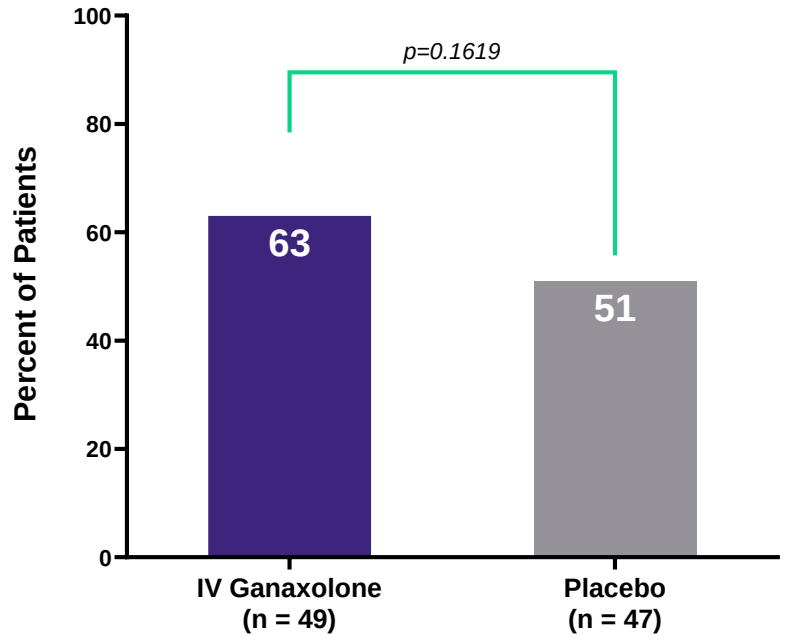
RAISE: Co-Primary Endpoints

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.

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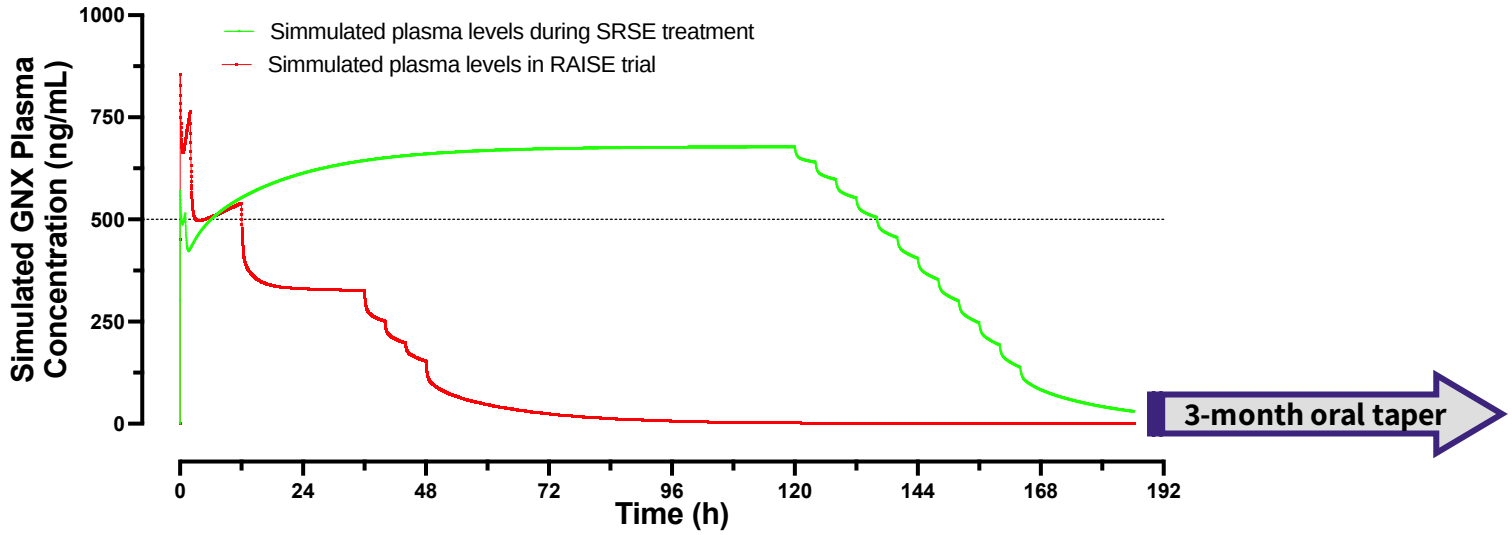
Approach to SRSE

29 patients with SRSE treated with IV ganaxolone as of May 2024
14 with regimen similar to RSE dosing
15 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



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Super Refractory Status Epilepticus: Ganaxolone Experience to Date

Ages

Age range	Number of patients
1-4 years	3
5-12 years	6
13-17 years	4
18 +	16
Total	29

Diagnoses

New onset refractory status epilepticus (NORSE)

Febrile illness-related epilepsy syndrome (FIRES)

Lennox-Gastaut syndrome

PCDH-19 related epilepsy

Autoimmune encephalitis

Herpes encephalitis

Vascular disorder

Mitochondrial disorder

Congenital malformation

Post-traumatic (remote)

Outcomes

Response	Prior regimen	New regimen	Total
SE resolution	5 (36%)	8 (53%)	13 (45%)
Partial response	6 (21%)	3 (20%)	6 (21%)
Did not respond	9 (43%)	3 (20%)	9 (31%)
Unknown	0	1 (7%)	1 (3%)
Total	14	15	29

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Financial Update

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Financial Overview

2024 Full Year Guidance

Revenues:

- U.S. ZTALMY Net Product Revenue: $33 - $35 million

Operating Expenses

- FY 2024 GAAP operating expenses (SG&A and R&D) of between $135 - $140 million; including ~$20 million of non-cash stock-based compensation

Financial Summary:

- $113.3 million in cash, cash equivalents, and short-term investments (at Mar. 31, 2024)
- Cash runway into Q2 2025
- $60 million in debt; matures 2026
- 54.9 million shares outstanding; 68.0 million shares on a fully dilutive basis[1] (at Mar. 31, 2024)

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.

[1] 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
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
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

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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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Appendix

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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 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

- 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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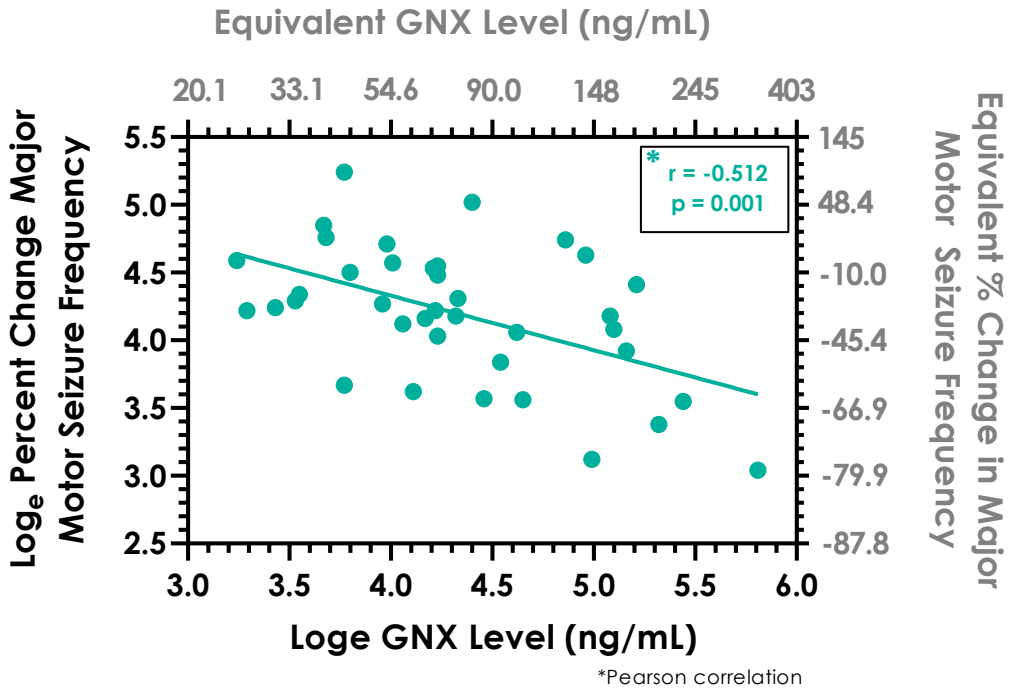
Average Ganaxolone Levels Correlate with Seizure Reduction

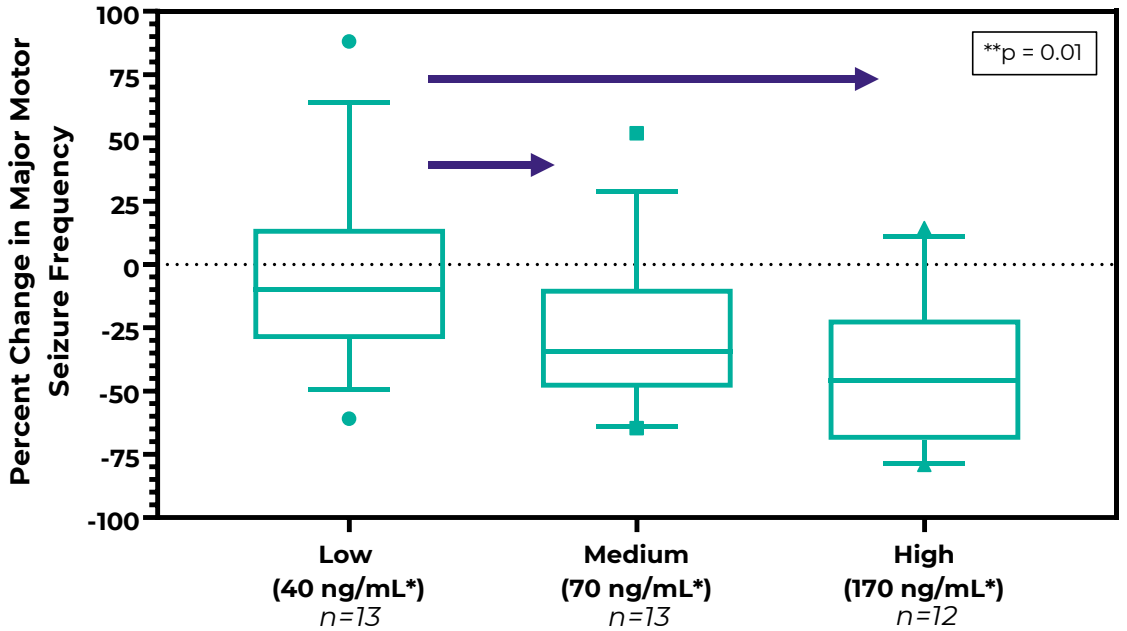
Marigold Study
CDKL5 Deficiency Disorder

- 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 ganaxlone dose level groups



*Pearson correlation

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



*mean GNX level within Group
**Kruskal-Wallis Test

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

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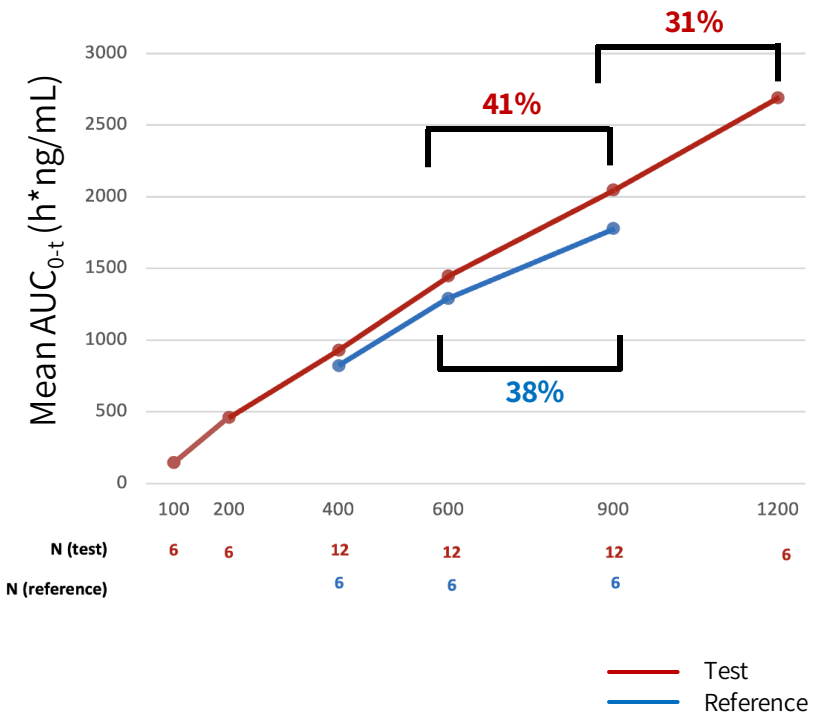
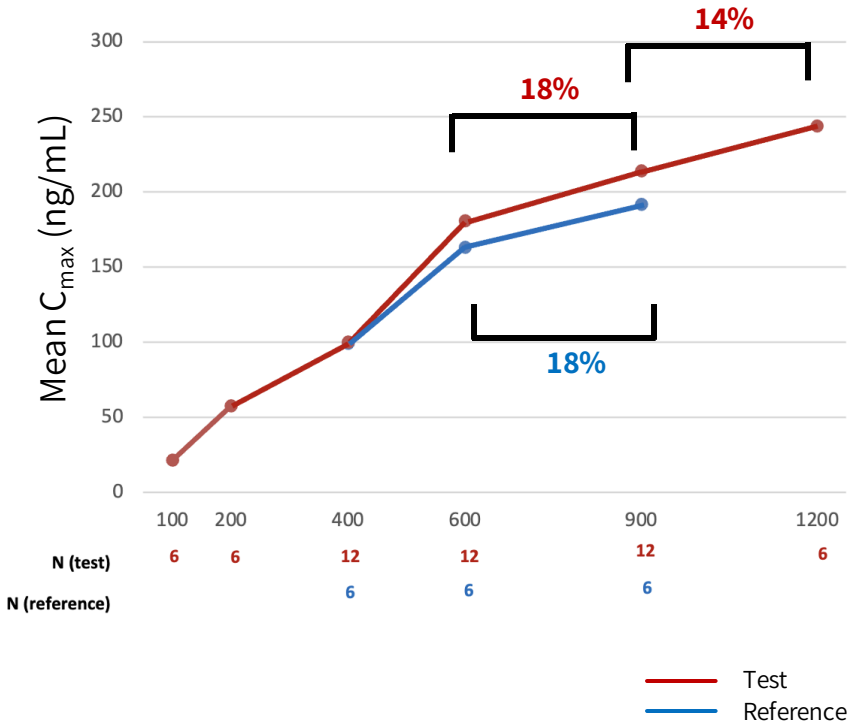
Phase 1 Single Ascending Dose (SAD) Study

Study design

- Single dose PK study in healthy adult volunteers
- Evaluated PK profile of 100, 200, 400, 600, 900 and 1200 mg of reformulated ganaxolone
- Ganaxolone reformulation administered as sprinkle mixed with water or yogurt





Ganaxolone reformulation demonstrated linear kinetics at single doses from 100-1200 mg

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Phase 2 Refractory Status Epilepticus Trial (RSE) Design

SE Patients

- Diagnosis of convulsive or non-convulsive SE
- Failed at least one 2nd line IV AED but had not progressed to 3rd line IV anesthetics

Screening →

Treatment Period			Post-treatment Follow-up	
Loading Dose	Maintenance	Taper	24 hour	Weeks 2, 3, 4
Bolus plus continuous infusion	2-4 day infusion	18-hour taper		

Cohort	Dose of ganaxolone/day	N
Low	500mg/day	5
Medium	650mg/day	4
High	713mg/day	8

17 patients enrolled

8 males, 9 females

Mean age: 57 years old (range: 23-88)

Goals of a new treatment

- Rapid cessation
- Maintenance of seizure control
- Prevent progression to IV anesthetics

Limitations of current treatments

- **1st line** Benzodiazepines ineffective in 45%-50%; limited by cardiovascular and respiratory side effects
- **2nd line** Ineffective in over 50% of established SE; further decreased response in refractory SE
- **3rd line** IV Anesthetics: high morbidity, mortality ~35%; increased duration of hospitalization and costs of care

Endpoints

- **Primary:** Percent of patients who did not require escalation of treatment with IV anesthetic within the first 24 hours after ganaxolone initiation
- **Secondary:** Additional efficacy, safety and tolerability

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Phase 2 Trial Results Demonstrated Rapid Onset And Durability of Effect

Cohort	No escalation to IV anesthetics within 24 hours from infusion initiation (Primary Endpoint)	Status-free through 24 hours from infusion initiation (investigator determination)	No escalation to additional IV AEDs or IV anesthetics for status relapse at any time through 24 hours after ganaxolone discontinuation	No SE Relapse at anytime during the 4-wk follow up period
High (713 mg/day) (n=8)	100% (8 of 8)	88% (7 of 8)	100% (8 of 8)	100% (6 of 6) (1ET, 1 died)
Medium (650 mg/day) (n=4)	100% (4 of 4)	100% (4 of 4)	75% (3 of 4)	67% (2 of 3) (1 ET)
Low (500 mg/day) (n=5)	100% (5 of 5)	100% (5 of 5)	60% (3 of 5)	50% (1 of 2) (1 died)

Trial data published in *Epilepsia*

Immediate Prior AED Administered 4 Hours (mean) to ganaxolone treatment

SE Cessation Occurred Rapidly in All Dose Groups (median = 5 minutes)

Safety Summary:

- 2 treatment emergent serious adverse events noted as severe sedation
- 13 treatment emergent adverse events: 5 moderate (4 somnolence; 1 hypercarbia); 6 mild (2 hypotension, 2 somnolence, 1 urinary retention, 1 hypercarbia)

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Data presented at AES 2019
AEDs – antiepileptic drugs

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