Topline Results from the Marigold Study:

Evaluating Ganaxolone for the Treatment of Seizures Associated with CDKL5 Deficiency Disorder

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September 14, 2020

Global Phase 3 Pivotal Trial Design

Marigold Study
CDKL5 Deficiency Disorder

Trial Details

- Evaluated the use of oral ganaxolone in children and young adults
- Global, double-blind, placebo-controlled, clinical trial enrolled 101 patients between the ages of 2 and 19 with a confirmed disease-related *CDKL5* gene variant
- Ages 2-19, ≥16 major motor seizures/month; up to 4 concomitant AEDs

Endpoints

- Primary endpoint of the trial was percent change in 28-day major motor seizure frequency *
- Non-seizure secondary outcome measures: Behavioral/neuropsychiatric changes correlated with domains of attention & sleep

* Major motor seizures were defined as bilateral tonic, generalized tonic-clonic, atonic/drop, bilateral clonic, or focal to bilateral tonic-clonic

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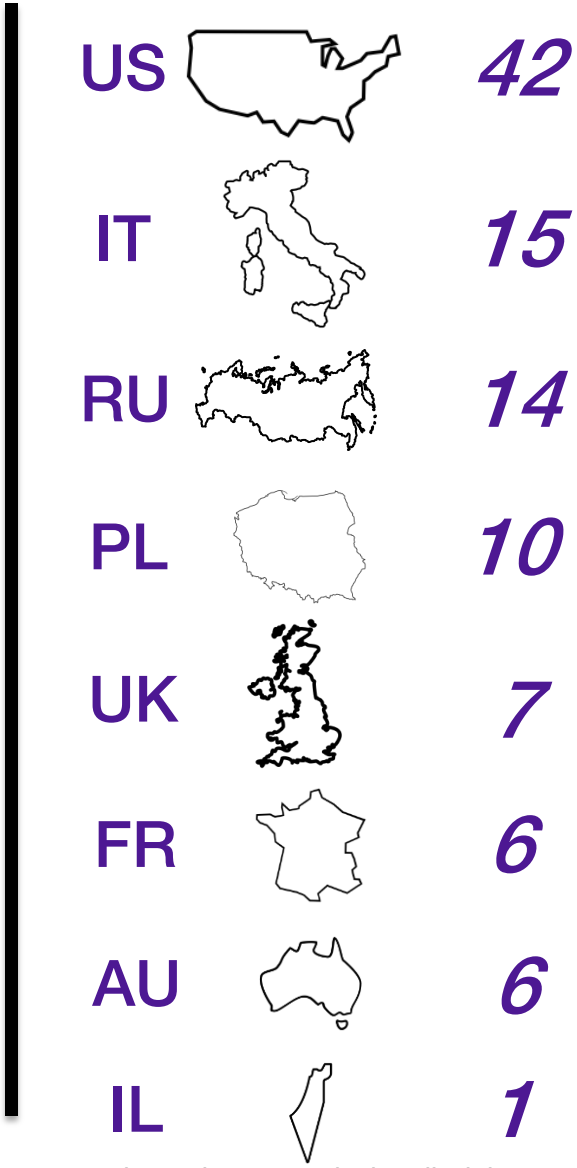
Subject Baseline Demographics & Country Enrollment in CDD Trial

Demographic	Placebo *(n=51)*	Ganaxolone *(n=50)*	Total *(n=101)*
Age, median	7.0	5.0	6.0
Gender, n (%)			
Male	10 (19.6)	11 (22.0)	21 (20.8)
Female	41 (80.4)	39 (78.0)	80 (79.2)
Ethnicity, n (%)			
Hispanic or Latino	6 (11.8)	4 (8.0)	10 (9.9)
Not-Hispanic or Latino	43 (84.3)	44 (88.0)	87 (86.1)
Unknown	1 (2.0)	1 (2.0)	2 (2.0)
Not reported	1 (2.0)	1 (2.0)	2 (2.0)
Race, n (%)			
White	47 (92.2)	46 (92.0)	93 (92.1)
Asian	3 (5.9)	2 (4.0)	5 (5.0)
Other	1 (2.0)	2 (4.0)	3 (3.0)



Subject Baseline Clinical Characteristics & Prior/Concomitant Medications

Characteristic	Placebo *(n=51)*	Ganaxolone *(n=50)*	Total *(n=101)*
Baseline Primary Seizure Frequency, per 28 days (median, min-mix)	50.0, 0.7 – 1021.3	57.3 5.5 – 651.3	-
Number of AED Medications Taken Prior (median)	7	7	7
Concomitant AED Medications, n (%)			
Valproate	16 (31.4)	18 (36.0)	34 (33.7)
Levetiracetam	13 (25.5)	13 (26.0)	26 (25.7)
Clobazam	13 (25.5)	12 (24.0)	25 (24.8)
Vigabatrin	12 (23.5)	10 (20.0)	22 (21.8)

Baseline seizure burden and AED history highlights unmet need

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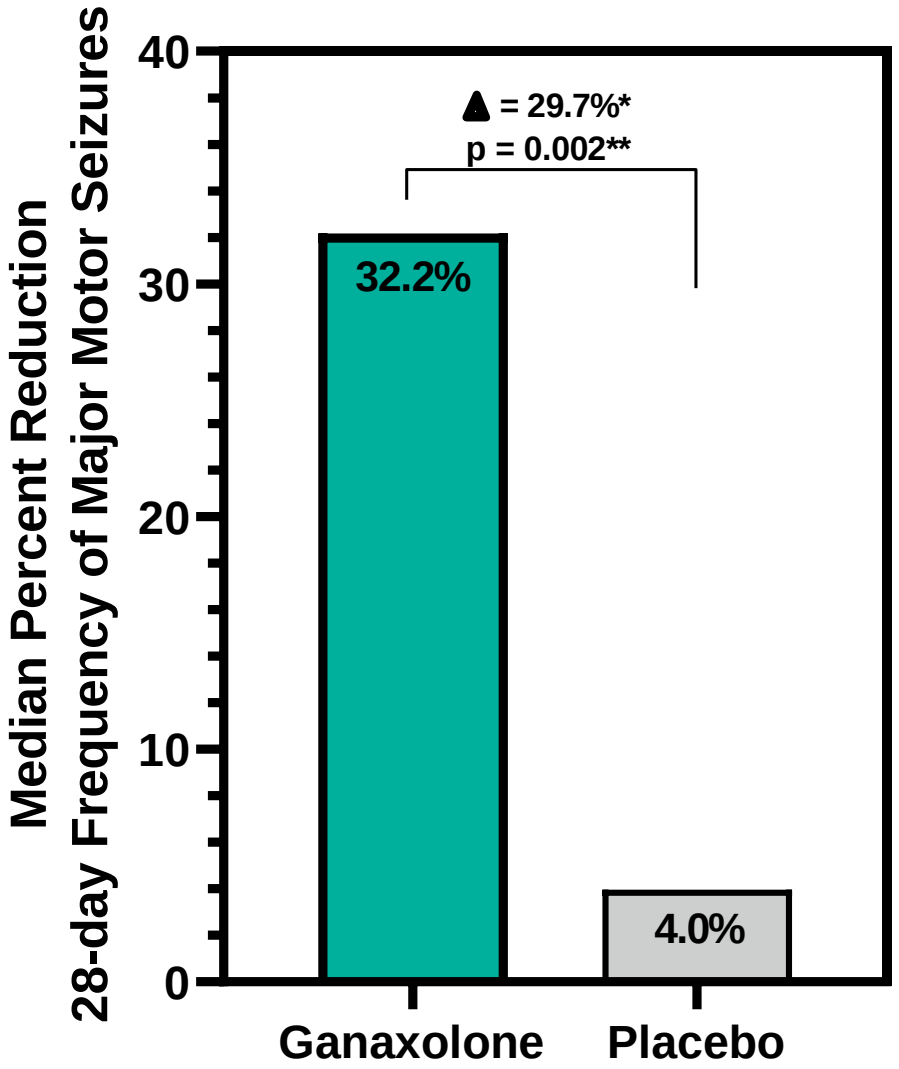
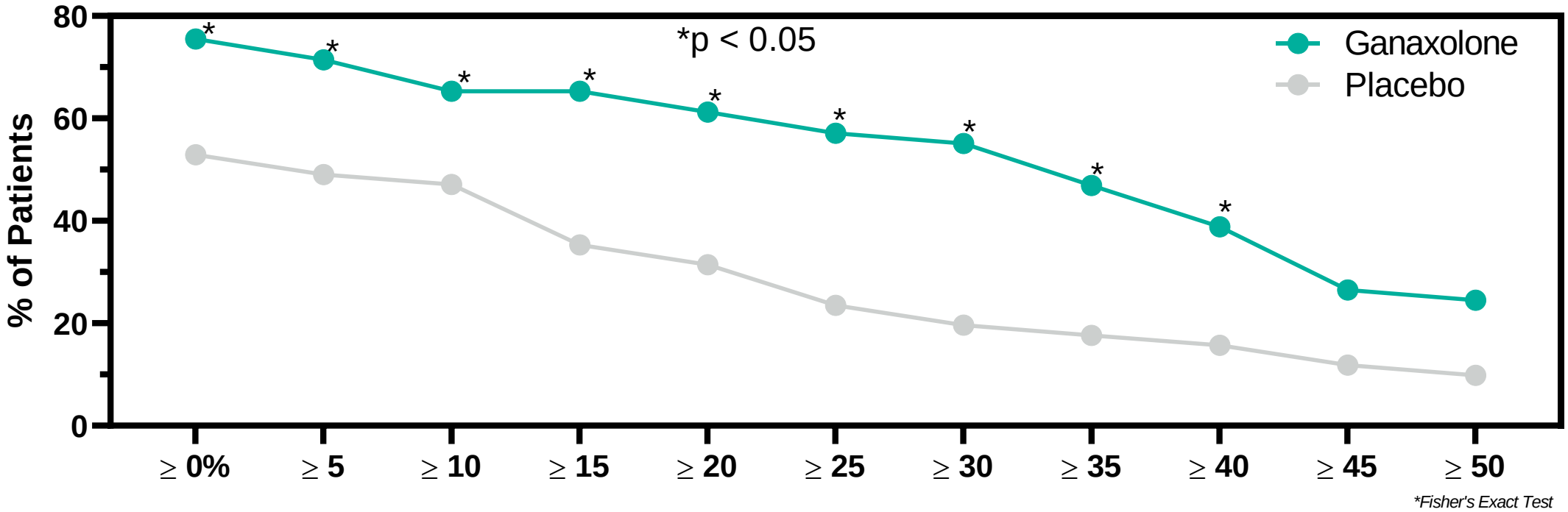
Ganaxolone Achieves Primary Efficacy Endpoint in the Marigold Study



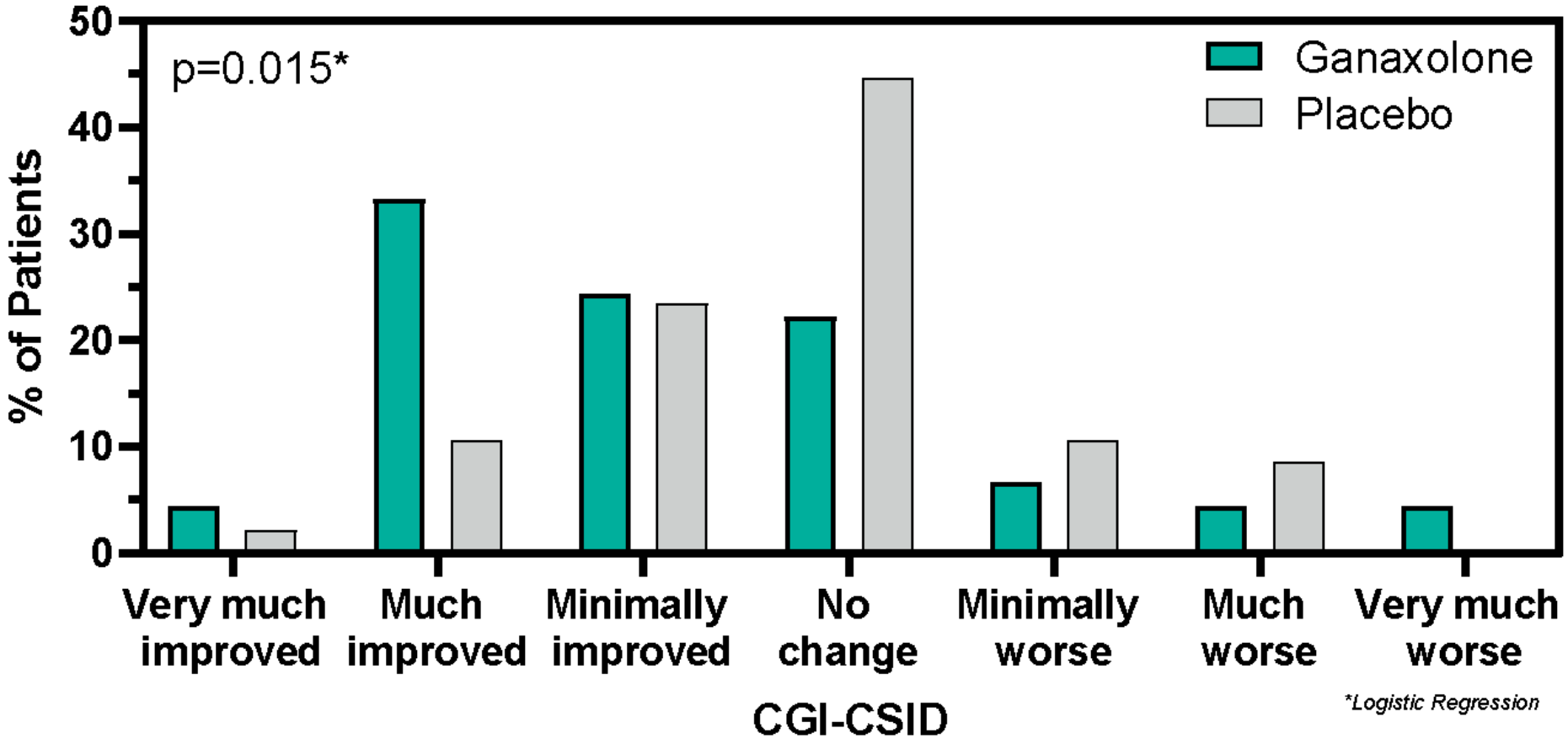
*Hodges-Lehman Estimate of Median Difference

**Wilcoxon Rank-Sum Test

Marigold Cumulative Response Curve



Caregiver Global Impression of Change in Seizure Intensity/Duration



Phase 3 Safety Summary

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)

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

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)

Summary of Safety Findings

- Ganaxolone was generally well tolerated and patients experienced less than a 5 percent discontinuation rate in the treatment arm
  - Somnolence was the most common adverse event.
- Serious adverse events (SAEs) were reported in 12% and 9.8% of ganaxolone and placebo treated patients, respectively
  - No clinically significant pattern of SAEs

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Q&A

