Intra-Cellular THERAPIES

April 16, 2024

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Study 501
Topline Results

Lumateperone as Adjunctive Therapy in Patients with Major Depressive Disorder

CAPLYTA (lumateperone) is FDA-approved for the treatment of depressive episodes associated with bipolar I or bipolar II disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate and for the treatment of schizophrenia in adults. The safety and efficacy have not been established for other uses.

Study 501 Topline Results

Study 501, Lumateperone adjunctive treatment study in patients with major depressive disorder who had an inadequate response to one or two antidepressants

Robust efficacy results

- Lumateperone 42 mg met the primary endpoint of change from baseline at Week 6 on the Montgomery-Åsberg Depression Rating Scale (**MADRS**) total score versus placebo **4.9 point reduction** v. placebo; **p<0.0001**; Cohen's d effect size **(ES)= 0.61**)
- Lumateperone 42 mg met the key secondary endpoint of change from baseline at Week 6 on the Clinical Global Impression Scale for Severity of Illness (**CGI-S**) (**p<0.0001; ES= 0.67**)

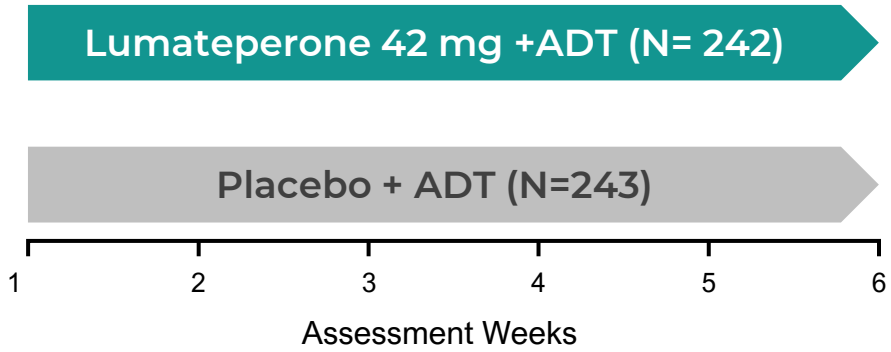
Favorable safety and tolerability profile generally consistent with prior lumateperone trials

Study 501 Study Design

Objective: To evaluate lumateperone 42 mg as adjunctive treatment in adult patients with MDD who are having inadequate response to antidepressant monotherapy (ADT)

Global, multicenter, randomized, double-blind, placebo-controlled clinical trial

Screening Period
Up to 2 weeks



Safety Follow-up
1 week

Key inclusion criteria

- 18 to 65 years of age
- Meet DSM-5 criteria for MDD
- MADRS ≥ 24; CGI-S ≥ 4; QIDS-SR-16 ≥ 14
- Inadequate response to ongoing ADT (<50% improvement)

Primary Endpoint

Mean change in MADRS total score at Week 6

Key Secondary Endpoint

Mean change in CGI-S at Week 6

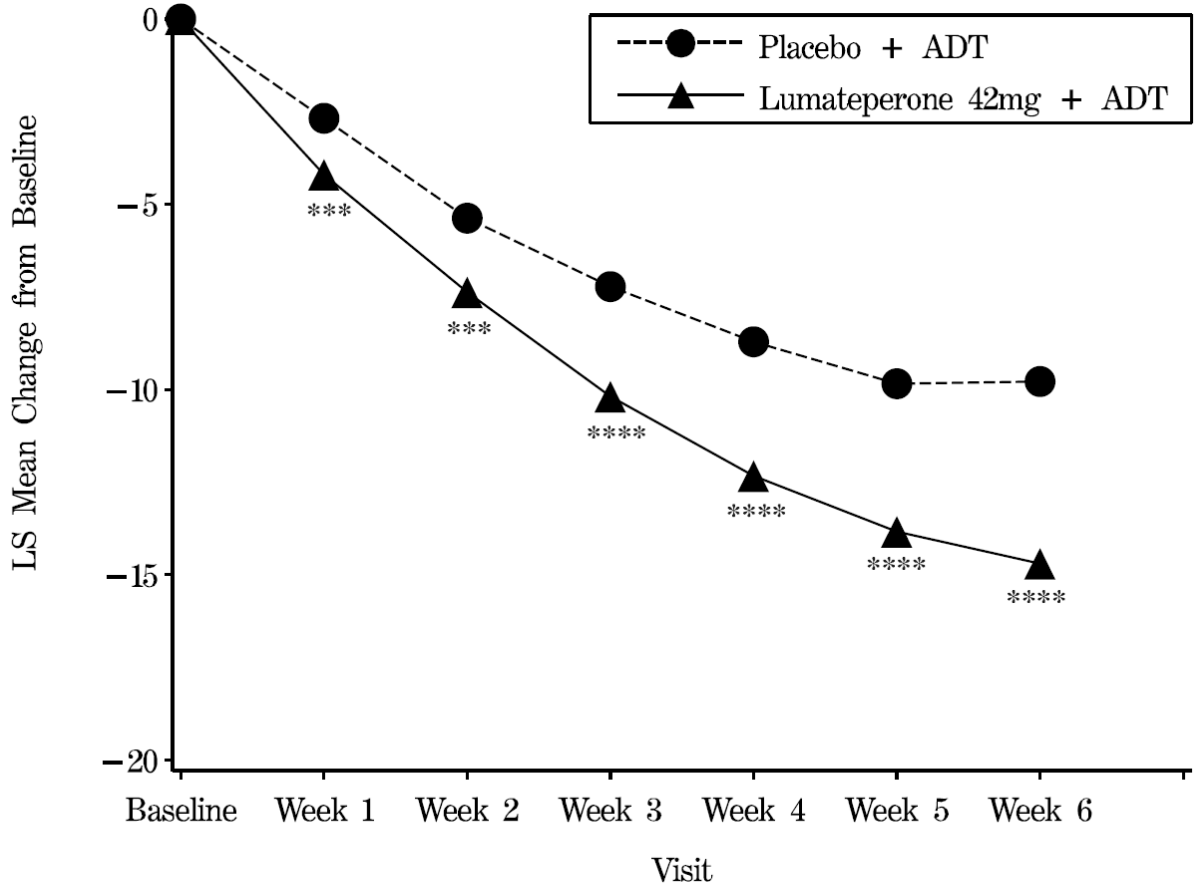
Demographics and Baseline Characteristics

	Lumateperone 42 mg + ADT (N=241)	Placebo + ADT (N=243)
Age (years), Mean ± SD	45.0 ± 12.39	45.1 ± 12.51
Gender, n (%)		
Male	83 (34.4)	83 (34.2)
Female	158 (65.6)	160 (65.8)
Race, n (%)		
White	180 (74.7)	191 (78.6)
Black or African American	20 (8.3)	16 (6.6)
Asian	40 (16.6)	33 (13.6)
Other	1 (0.4)	3 (1.2)
Mean Baseline MADRS Score	30.4	30.0
Mean Baseline CGI-S Score	4.7	4.6

MADRS= Montgomery-Åsberg Depression Rating Scale, CGI-S = Clinical Global Impression Scale

Lumateperone Demonstrated a Statistically Significant Reduction on the MADRS Total Score Compared to Placebo at Week 6

MADRS Total Score



LS mean difference vs placebo

-4.9 points

p < 0.0001

(actual p=0.0000000001413)

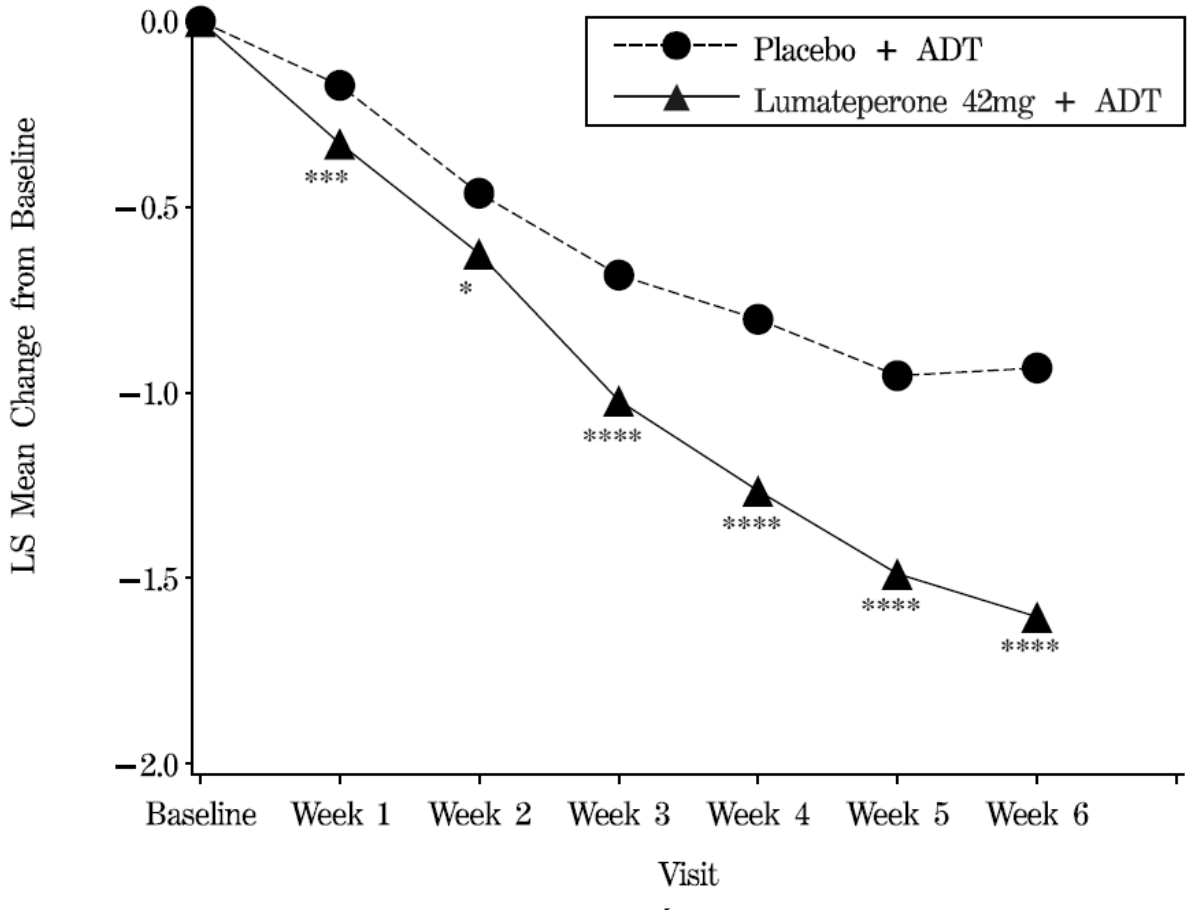
Cohen's d effect size:

0.61

mITT population: Lumateperone N=239, Placebo N=242
***p<0.001 ****p<0.0001

Lumateperone Demonstrated a Statistically Significant Reduction on the CGI-S Score Compared to Placebo at Week 6

CGI-S Score



p < 0.0001

(actual p=0.0000000000046)

Cohen's d effect size:

0.67

mITT population: Lumateperone N=239, Placebo N=242
*p<0.05 ***p<0.001 ****p<0.0001

Lumateperone Robustly Improved Depressive Symptoms as Reported by Patients

Change From Baseline to Day 43 in QIDS-SR-16 Total Score

Measurement Statistics	Lumateperone 42 mg + ADT (N=241)	Placebo + ADT (N=243)
Baseline, Mean (SD)	18.1 (2.31)	17.6 (2.28)
Change from Baseline to Day 43		
n	236	238
LS Mean (SE)	-8.0 (0.33)	-5.6 (0.33)
LSMD vs Placebo (SE)	-2.4 (0.44)	—
95% CI	(-3.23, -1.51)	—
P-Value	<0.0001 (actual p=0.0000000987146)	—

QIDS-SR-16: Quick Inventory of Depressive Symptomatology Self Report

Favorable Safety and Tolerability Profile Generally Consistent with Prior Lumateperone Trials

- Overall discontinuation rate was 6.6% (lumateperone 8.7%, placebo 4.5%)
- Overall treatment emergent adverse events (TEAEs): lumateperone 58.1% and placebo 46.1%
- Discontinuation rates due to TEAEs: lumateperone 5.8% and placebo 0.8%
- Most common adverse events (≥ 5% lumateperone group and twice placebo): dry mouth (10.8%), fatigue (9.5%), and tremor (5.0%). Adverse events were mostly mild to moderate and resolved within a short period of time
- One serious adverse event reported in placebo group during the double-blind treatment period

Study 501 Conclusions

In this adjunctive treatment study in patients with major depressive disorder who had an inadequate response to one or two antidepressants

- Lumateperone 42 mg plus antidepressant demonstrated **robust efficacy over placebo plus antidepressant on primary endpoint** (MADRS total score) **and key secondary endpoint** (CGI-S score)
- Lumateperone 42 mg plus antidepressant was generally **safe and well tolerated in patients with MDD**
  - Adverse event safety profile in the MDD population was generally consistent with existing lumateperone safety profile in schizophrenia and bipolar depression

Thank you