

# Corporate Presentation

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May 2019





# Safe Harbor Statement

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements concern our product candidates, our development efforts, our collaborations, our technology, our intellectual property, our financial condition, our plans and our development programs. These statements involve risks, uncertainties and assumptions, and are based on the current estimates and assumptions of the management of Intra-Cellular Therapies, Inc. (the “Company” or “ITCI”) as of the date of this presentation and are subject to uncertainty and changes. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, those set forth in our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the Securities and Exchange Commission, as well as any updates to those risk factors filed from time to time in our periodic and current reports. All statements contained in this presentation are made only as of the date of this presentation, and the Company undertakes no duty to update this information unless required by law.



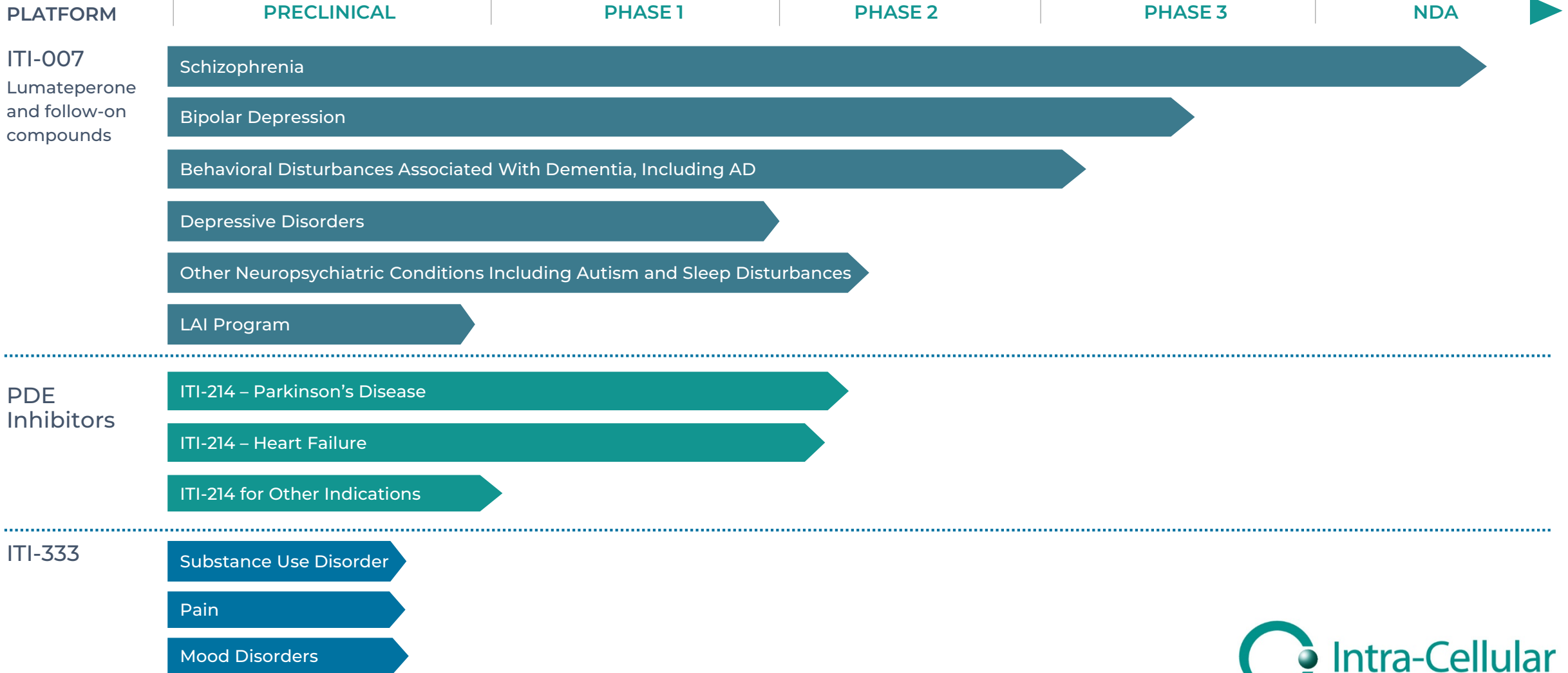
# Intra-Cellular Therapies, Inc. (ITCI)

- Founded in 2002, leveraging technology to study intracellular signaling from the lab of Nobel Laureate Dr. Paul Greengard
- Focus on advancements in the treatment of CNS disorders
  - Lead program: Lumateperone (ITI-007)
    - For the treatment of schizophrenia
      - NDA under FDA review, PDUFA target action date September 27, 2019
    - For the treatment of bipolar depression
  - Leader in the field of PDE1 inhibitors
    - Parkinson's disease
    - Heart failure
- Well-capitalized
  - \$312.8 million in cash, cash equivalents and investment securities at 3/31/2019





# ITCI Therapeutic Pipeline



# Schizophrenia Is a Common Disabling Neuropsychiatric Disease



Schizophrenia affects ~1% of the global population<sup>1</sup>

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2.4 million adults in the United States have schizophrenia<sup>2</sup>

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Economic burden of schizophrenia exceeds \$154 Billion in the U.S.<sup>3</sup>

- Onset in early adulthood leads to life-long disability
- It is estimated that only about one-third of patients with schizophrenia can work regularly<sup>4</sup>

1. National Alliance on Mental Illness. <https://www.nami.org/Learn-More/Mental-Health-Conditions/Schizophrenia>. Accessed Dec 28, 2018.

2. National Institutes of Health. <https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=67> Accessed Dec 28, 2018.

3. Cloutier M, et al. *J Clin Psychiatry*. 2016;77(6):764-771.

4. Bellack AS, et al. *Schizophr Bull*. 2007;33(3):805-822.

# Lumateperone Is Designed to Address Unmet Needs in Schizophrenia



- Existing therapies are associated with significant adverse events, including extrapyramidal symptoms, akathisia, metabolic disturbances, weight gain and cardiovascular dysfunction
  - Impact quality of life
  - Lead to poor adherence, with 74% of US patients discontinuing medication within 18 months<sup>1</sup>
- Existing drugs are:
  - Only effective for positive symptoms; negative symptoms and depression are not effectively treated
  - Social function is not improved



Weight loss and improvement in key cardiometabolic parameters were observed with long-term treatment with lumateperone vs Standard of Care (SOC)



The unique pharmacology of lumateperone may translate into an advancement in the treatment of schizophrenia as a single, stand-alone drug therapy



# Lumateperone: Novel, First-in-Class Molecule With an MOA That Predicts Clinical Benefits Across CNS Disorders

	$K_i$ (nM)
5-HT <sub>2A</sub>	0.5
D <sub>2</sub>	32
D <sub>1</sub>	52
SERT	62

## 5-HT<sub>2A</sub> Receptor Antagonist

- Improves sleep quality
- Reduces anxiety and hostility
- Enhances antipsychotic and antidepressant activity

## Glutamatergic Phosphoprotein Modulator

- NMDA & AMPA Enhancement via D<sub>1</sub>
- Efficacy for negative and positive symptoms
  - Improved cognition
  - Rapid-acting antidepressant activity

## Dopamine Phosphoprotein D<sub>2</sub> Modulator (DPPM)

- D<sub>2</sub> pre-synaptic partial agonist and post-synaptic antagonist
- Antipsychotic efficacy for positive symptoms
  - Reduced agitation

PHARMACOLOGY PREDICTS ROBUST EFFICACY ACROSS A BROAD RANGE OF SYMPTOM DOMAINS

AND PREDICTS HIGHLY FAVORABLE SAFETY/TOLERABILITY PROFILE

## Serotonin Reuptake Inhibitor

- Antidepressant activity



# Lumateperone Schizophrenia Program Overview

- Lumateperone (ITI-007 60 mg) met primary efficacy endpoint in 2 entirely U.S. based studies
- Well-tolerated with a safety profile similar to placebo in all studies
- Once daily oral dosing with no need for titration to 60 mg
- Two studies with risperidone as active control showed statistically significant safety and tolerability benefits for lumateperone over risperidone
- NDA under FDA review, PDUFA target action date September 27, 2019

## 3 Large Randomized, Double-Blind Trials

Primary outcome measure: change from baseline on Positive and Negative Syndrome Scale (PANSS) Total Score

### ITI-007-005<sup>1</sup>

4-week treatment period  
N=335

- ITI-007 (60 mg or 120 mg)
- Risperidone 4 mg or
- Placebo

### ITI-007-301

4-week treatment period  
N=450

- ITI-007 (60 mg or 40 mg) or
- Placebo

### ITI-007-302

6-week treatment period  
N=696

- ITI-007 (60 mg or 20 mg)
- Risperidone 4 mg or
- Placebo

## Open-Label Safety Switching Study - ITI-007 60 mg

### First Part

6-week treatment duration  
N=302

### Second Part

Long-term treatment

ICH guidelines met  
300 pts for 6 mos., 100 for 1 yr



1. Lieberman JA et al., *Biological Psychiatry*. 2016;79(12):952-961.



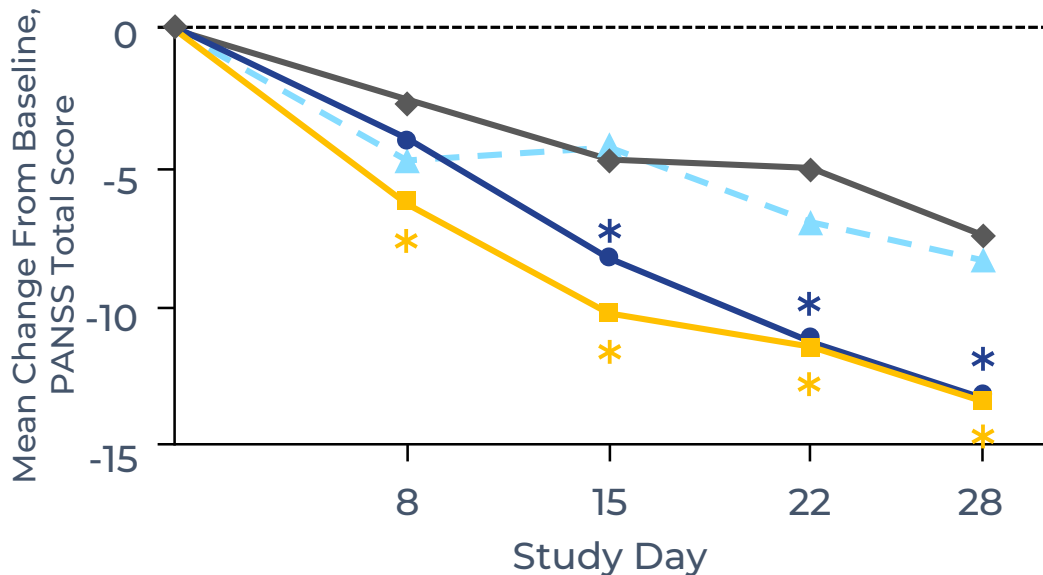
# ITI-007 60 mg Met Primary Endpoint in 2 Positive Large Schizophrenia Studies



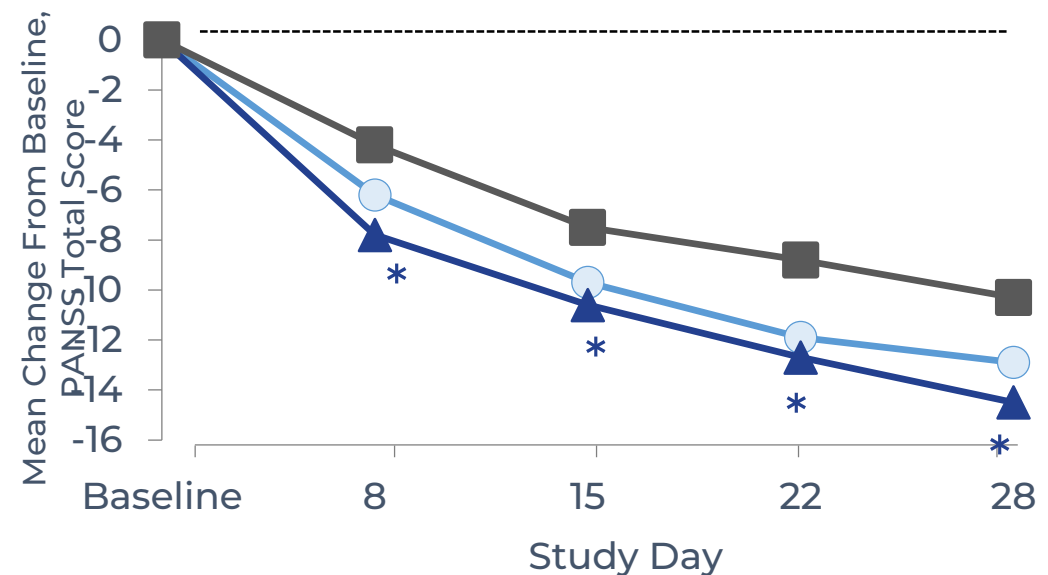
ITI-007-005

ITI-007-301

## Mean Change From Baseline in PANSS Total Score



- Lumateperone 60 mg (n=76)
- ▲ Lumateperone 120 mg (n=80)
- Risperidone 4 mg (n=75)
- ◆ Placebo (n=80)

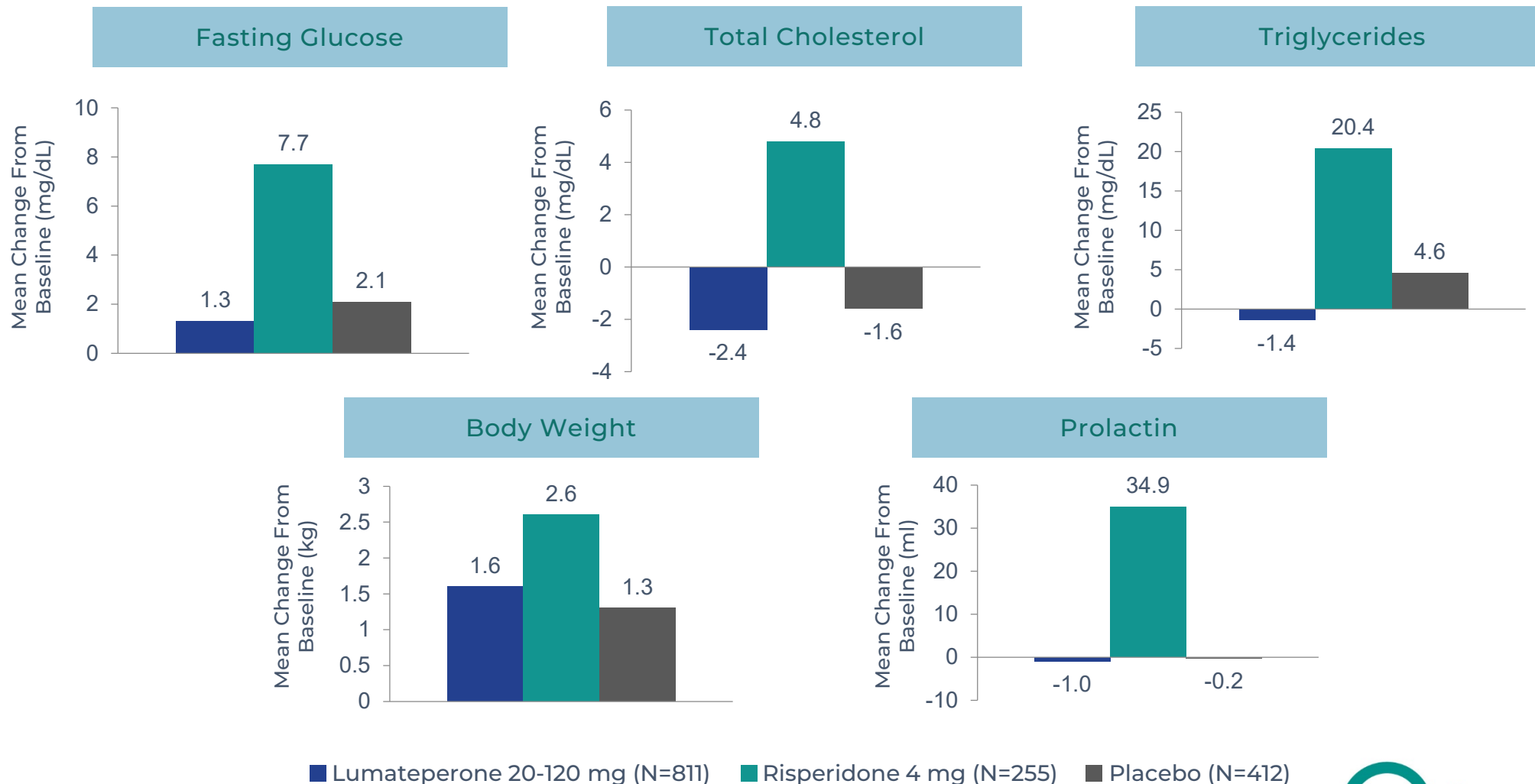


- Lumateperone 40 mg (n=146)
- ▲ Lumateperone 60 mg (n=148)
- Placebo (n=141)

\* $P < .05$  vs placebo.

PANSS=Positive and Negative Syndrome Scale.

# Pooled Data from 3 Acute Controlled Studies Demonstrated the Favorable Safety Profile of Lumateperone: Similar to Placebo and Superior to Risperidone on Key Safety Parameters

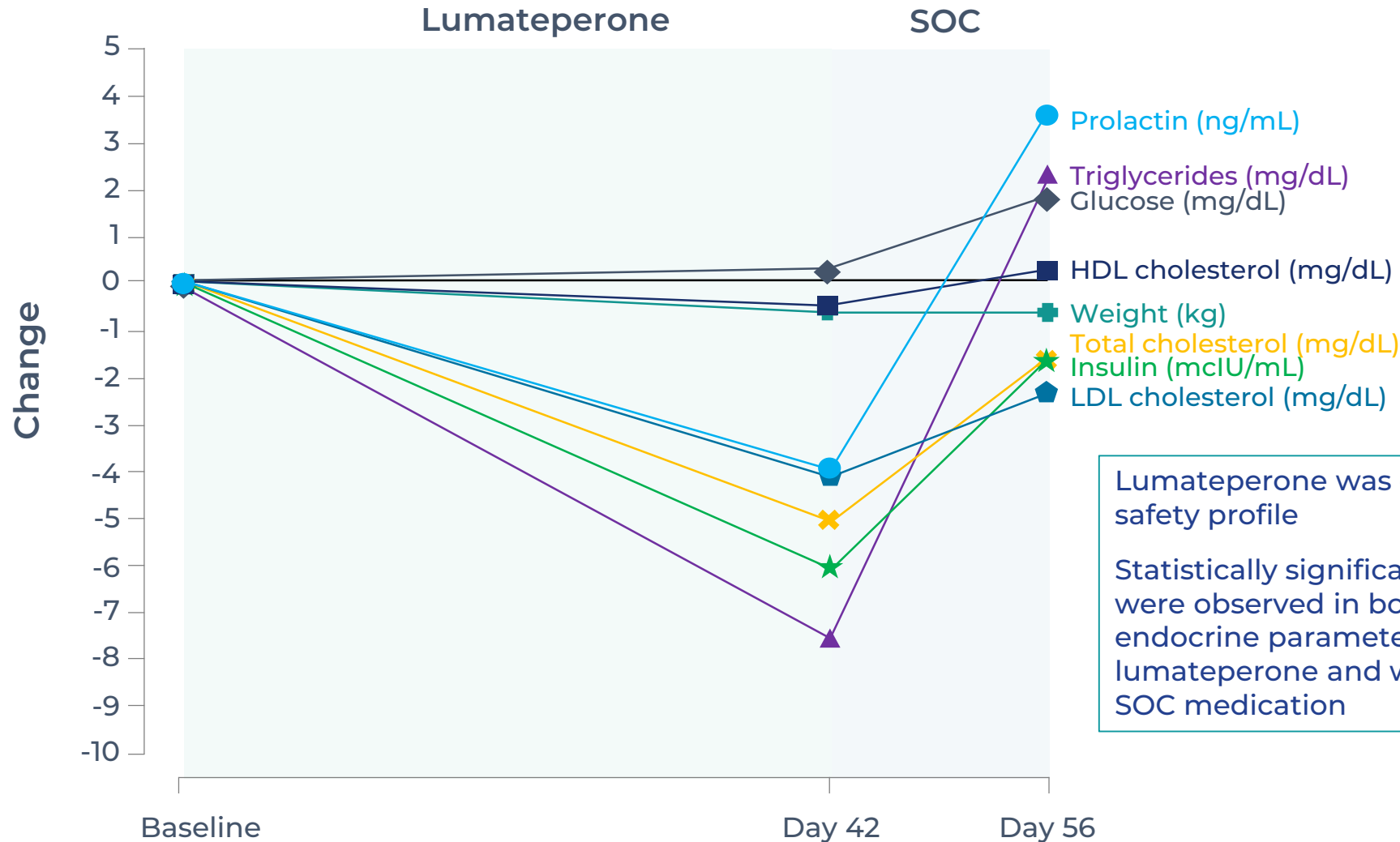


# Lumateperone Profile Confirmed in Open-Label Safety Switching Study (Study 303) in Patients With Stable Schizophrenia Symptoms



- The study evaluated the safety of lumateperone 60 mg in stable patients with schizophrenia in an outpatient setting similar to common clinical practice
- Part 1: 6-week treatment duration assessed:
  - The impact of switching to lumateperone from SOC antipsychotics (with no dose titration necessary for lumateperone)
  - The impact of switching back to SOC from lumateperone
- Part 2: Up to 1-year treatment duration assessed:
  - The long-term impact of switching to lumateperone from SOC antipsychotics (with no dose titration necessary for lumateperone)

# PART 1: 6-Week Open-Label Safety Switching Study, Key Cardiometabolic Parameters Improved on Lumateperone and Worsened Again After Switch Back to SOC (N=302)



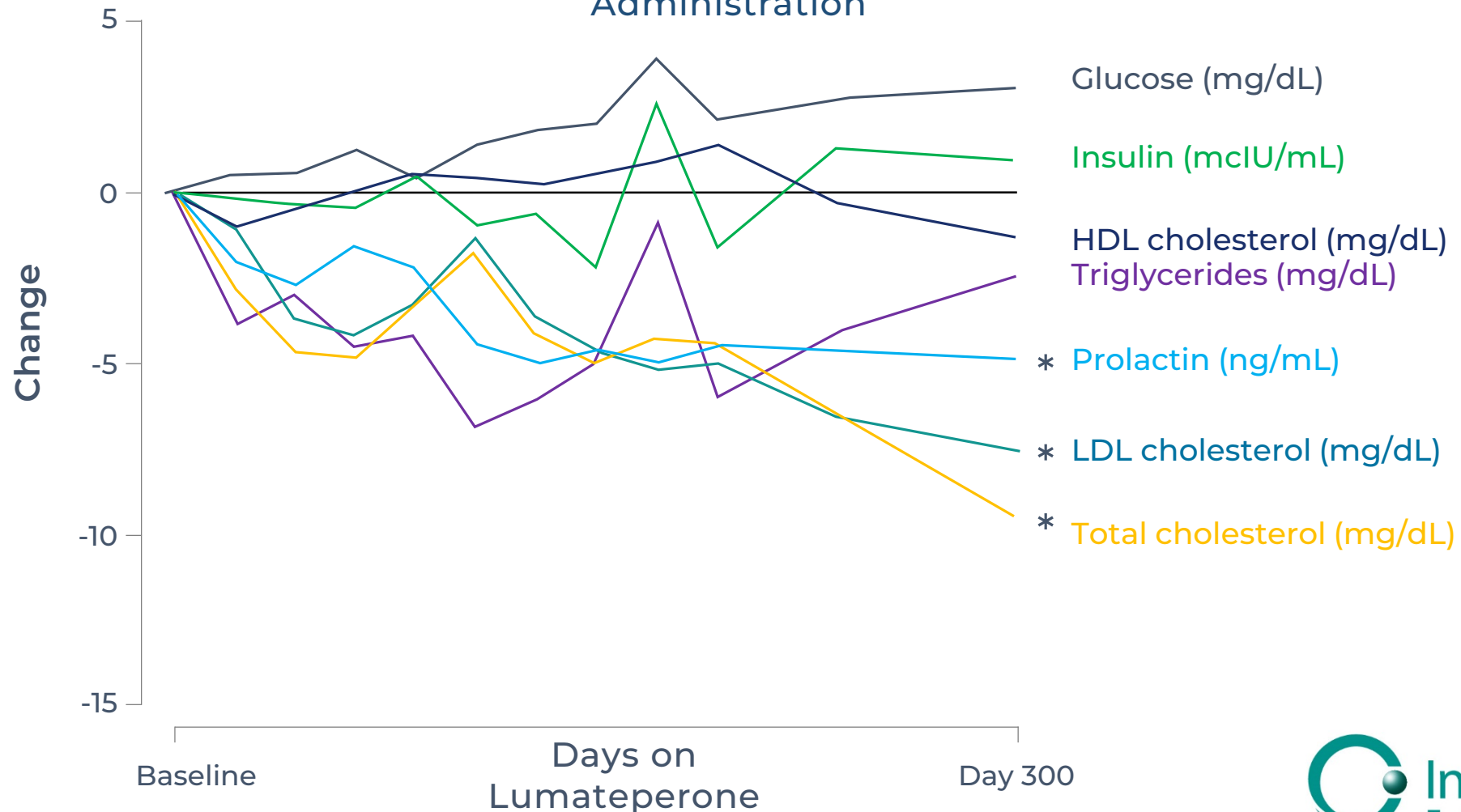
Lumateperone was generally well tolerated with a favorable safety profile

Statistically significant improvements from SOC baseline were observed in body weight, cardiometabolic and endocrine parameters over 6 weeks of treatment with lumateperone and worsened again when switched back to SOC medication

# PART 2: Open-Label Long-Term Study, Key Cardiometabolic Parameters Improved on Lumateperone



Lumateperone Exhibited a Favorable Cardiometabolic Profile with Long-Term Administration

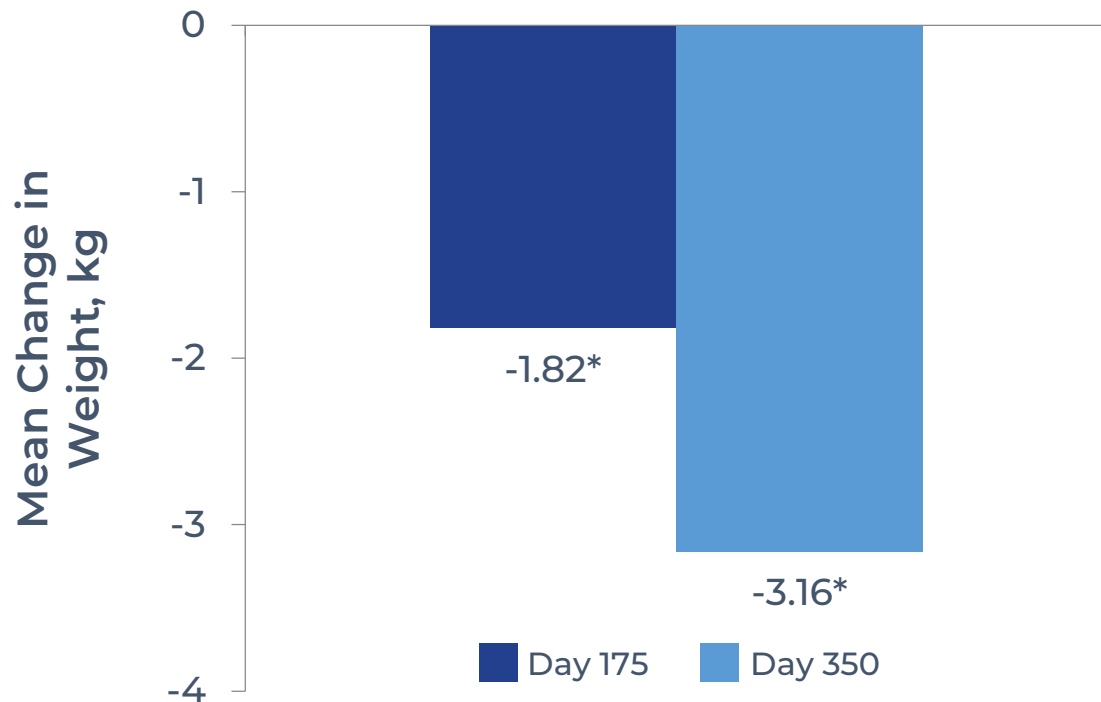


\* $P < .001$  vs baseline. Results meeting ICH guidelines for long-term safety presented at ACNP 2018 on 329 patients treated for at least 6 months and 108 patients treated for 1 year.

# Open-Label Long-Term Study, Weight Decreased on Lumateperone



### Change in Body Weight



### Patients With Significant Change in Weight ( $\geq 7\%$ ) at Any Time During the Study

Weight decrease	24%
Weight increase	8%

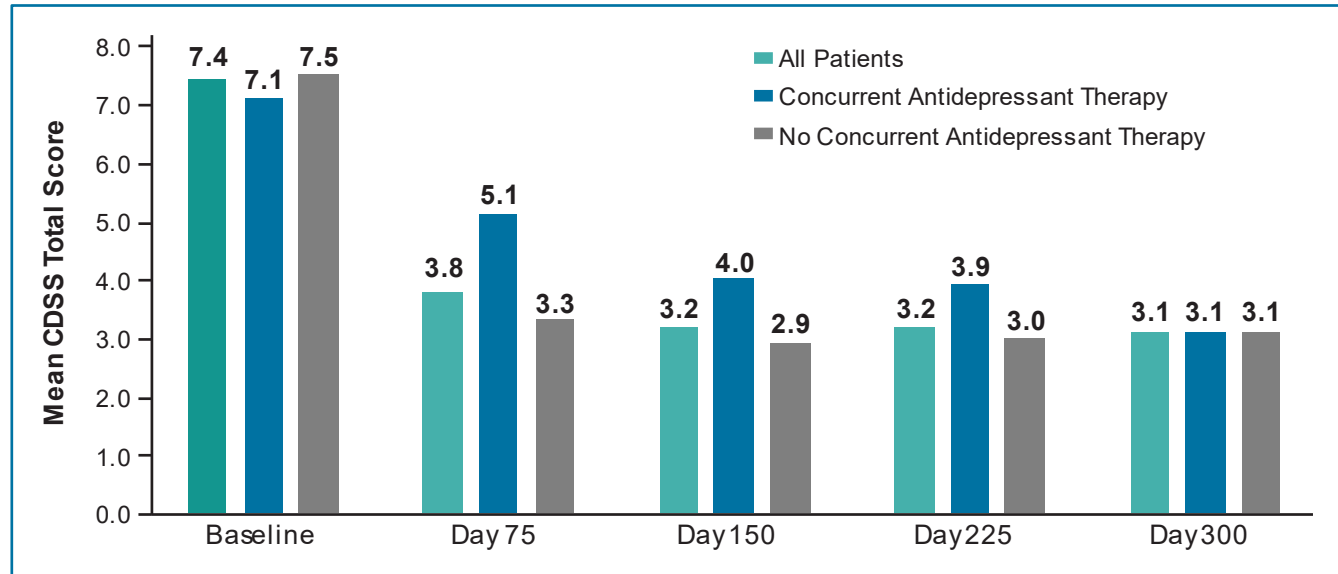
\* $P < .01$  compared to SOC baseline.

Results meeting ICH guidelines for long-term safety presented at ACNP 2018 on 329 patients treated for at least 6 months and 108 patients treated for 1 year. At baseline, the mean body weight was 92.5 kg.

# In Patients with Co-morbid Depression at Baseline Lumateperone Improved Depression Symptoms



CDSS Total Score Over Time in Schizophrenia Patients with Comorbid Depression at Baseline<sup>a</sup>



<sup>a</sup>In patients with CDSS score >5 at baseline and post-baseline CDSS assessments (n = 55)  
CDSS, Calgary Depression Scale for Schizophrenia

- CDSS scores decreased by ~60% from 7.4 at baseline to 3.1 at Day 300
- Response ( $\geq 50\%$  reduction from baseline in CDSS Total score) was achieved by 60% of patients by Day 75 and maintained through Day 300
- Improvements in depression symptoms were seen in seen patients who were taking antidepressant therapy and patients who were not on antidepressants



# Summary: Lumateperone Schizophrenia Program

- Program includes 2 large, well-controlled positive studies and supportive data from a third study
- In all 3 studies, lumateperone was well-tolerated with a safety profile similar to placebo
- In the 2 studies with risperidone as the active control, lumateperone was statistically significantly better than risperidone on key safety and tolerability parameters
- Long-term safety study confirmed the favorable cardiometabolic safety profile demonstrated in short-term studies. Weight loss seen in short-term studies continued over long-term treatment



# Our Commercial Leadership Team Has Extensive Biopharma Experience



Mark Neumann, EVP,  
Chief Commercial Officer

John Bardi, SVP, Market Access, Policy  
& Government Affairs

Debra Marchese, VP, Marketing

George Rodriguez, VP, Sales

Jennifer Rinaldo, VP, Strategy & Commercial  
Development



135 Combined years of experience





# Bipolar Depression Is a Common Psychiatric Condition

- Bipolar disorder has a 12-month prevalence of 2.8% in US adults<sup>1</sup>
  - Affects ~6 million Americans<sup>2</sup>
  - Bipolar depression is the predominant presentation
  - Depressive episodes are longer and recur more often than manic/hypomanic episodes
  
- Unmet need
  - Few approved treatments available
  - Safety and tolerability tradeoff limits use of existing agents

1. National Institute of Mental Health. Bipolar Disorder. [https://www.nimh.nih.gov/health/statistics/bipolar-disorder.shtml#part\\_155458](https://www.nimh.nih.gov/health/statistics/bipolar-disorder.shtml#part_155458). Accessed Dec 28, 2018.

2. Depression and Bipolar Support Alliance. [https://secure2.convio.net/dabsa/site/SPageServer/?pagename=education\\_bipolar](https://secure2.convio.net/dabsa/site/SPageServer/?pagename=education_bipolar). Accessed Jan 3, 2019.

# Lumateperone for the Treatment of Bipolar Depression and Other Depressive Disorders

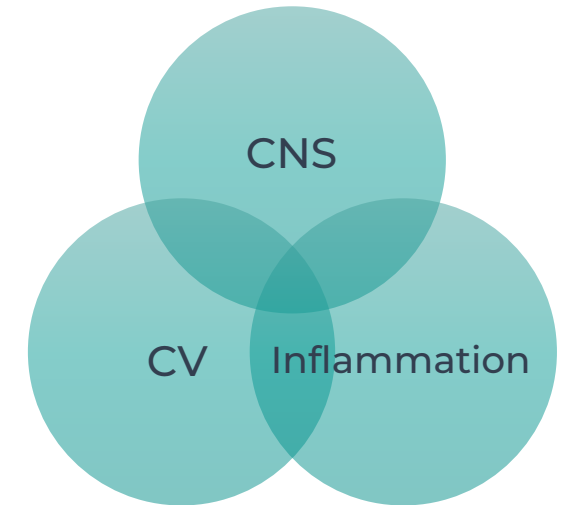


- Potent 5-HT<sub>2A</sub> receptor antagonism and D<sub>2</sub> receptor modulation, coupled with inhibition of serotonin transporters and enhancement of glutamatergic neurotransmission, suggest antidepressant activity
  - In previous studies, depressed patients with schizophrenia experienced robust improvements in depressive symptoms
  - Preclinical data support potential for rapid-acting antidepressant effects
- Bipolar depression phase 3 clinical program includes
- Two monotherapy studies
  - One adjunctive study (lithium or valproate)
- Program in major depressive disorder (MDD)
- Objective: evaluate antidepressant effects on lumateperone including rapid-onset effects
  - Novel formulations being assessed to explore the effect of different modes of drug administration and the potential for rapid-onset antidepressant activity

# PDE1 Inhibition: Novel Approach to Modulation of Intracellular Signaling With Broad Therapeutic Potential



- PDE1 enzymes are highly active across a variety of neurological and cardiovascular diseases
- Our PDE1 inhibitors are designed to reestablish normal function in these disease states
  - Inhibitors of PDE1 block the breakdown of cyclic nucleotides (cAMP, cGMP) potentiating downstream intracellular signaling
- ITI-214, our lead PDE1 molecule, is being developed for the treatment of Parkinson's disease and heart failure





# ITI-214 for the Treatment of Parkinson's Disease (PD)

- Over 2.2 million patients in the US and Europe<sup>1,2</sup>
- Unmet need
  - Progressive neurodegenerative disorder with motor and non-motor symptoms
  - Dopamine replacement therapies (L-DOPA as gold standard) address motor symptoms, but are insufficient and have limiting side effects
  - Effects of dopamine replacement therapies wear off over time as disease progresses
- ITI-214 is a multi-pronged approach to the treatment of PD
  - PDE1 inhibition/ITI-214 enhances intracellular dopamine signaling pathways in the brain
  - ITI-214 may be neuroprotective and has potential disease-modifying effects

1. Parkinson's Foundation. <https://www.parkinson.org/Understanding-Parkinsons/Statistics>. Accessed Jan 3, 2019.

2. European Parkinson's Disease Association. [http://ec.europa.eu/research/horizon2020/pdf/contributions/post/european\\_organisations/european\\_parkinson%27s\\_disease\\_association\\_-\\_epda.pdf](http://ec.europa.eu/research/horizon2020/pdf/contributions/post/european_organisations/european_parkinson%27s_disease_association_-_epda.pdf). Accessed Jan 3, 2019.



# ITI-214 Phase 1/2 Results in PD

- Study ITI-214-105
  - A Phase 1/2, placebo-controlled, multiple ascending dose cohort study in patients with mild to moderate PD maintained on stable (concomitant) PD medication
  - Patients randomly assigned to receive placebo or ITI-214 (1, 3, 10, 30, and 90 mg) administered orally once daily for 7 days
- ITI-214 was shown to have a favorable safety profile and was generally well tolerated
  - Across a broad range of doses (1 mg to 90 mg)
  - Without promoting or worsening motor complications
- Clinical signs consistent with reductions in motor symptoms and motor complications
  - Signals of motor improvement seen in the MDS-UPDRS (and Subscales Part III and Part IV)
  - Reduced dyskinesia symptoms seen in UDysRS and increase in “ON” time without dyskinesia (Hauser Patient Motor Diary) in patients with dyskinesia at baseline
  - Several patients experienced profound improvements

# ITI-214 Represents A Novel Mechanism of Action for the Treatment of Heart Failure



- Heart failure affects approximately 5.8 million people and has a mortality rate of ~50% within 5 years<sup>1</sup>
  - Need for approaches that improve heart function acutely and with longer exposure, also counter maladaptive remodeling of the ventricle
- Preclinical data have shown beneficial effects on cardiac function
  - PDE-1 inhibition increases cardiac contractility and cardiac output
  - Potential for attenuation or reversal of cardiac remodeling
  - ITI-214 acts by a novel mechanism of action that involves modulation of adenosine A<sub>2B</sub> receptor signaling pathways
- Ongoing translational study: a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 in patients with systolic heart failure to evaluate contractility and pharmacodynamic parameters
  - Clinical conduct for the second cohort, 30 mg, is ongoing following completion of the 10 mg dose cohort where no safety concerns were identified

# ITI-333: For the Treatment of Substance Use Disorders, Pain, and Mood Disorders



- Opioid crisis is a public health emergency
  - Nearly 12 million people in the United States misused opioids in the previous year<sup>1</sup>
  - 130+ people a day die from opioid-related drug overdoses<sup>2</sup>
- ITI-333 profile

Receptor or Transporter	K <sub>i</sub> (nM)
Serotonin 5-HT <sub>2A</sub>	8.3
Dopamine D <sub>1</sub>	50
Mu opioid (MOP)	11

- High affinity at serotonin 5-HT<sub>2A</sub>, dopamine D<sub>1</sub>, and mu opioid receptors (MOP), acting as a partial agonist at MOP receptors
- Exhibits potent morphine-like analgesia in animal models, yet attenuates several morphine-mediated behaviors (eg, does not cause respiratory depression or loss of GI motility)
- No safety concerns have been noted with ITI-333 in animal models

1. Substance Abuse and Mental Health Services Administration. (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health (HHS Publication No. SMA 17-5044, NSDUH Series H-52). <https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>. Accessed Jan 3, 2019.

2. U.S. Department of Health and Human Services. <https://www.hhs.gov/opioids/>. Accessed Jan 3, 2019.





# Management Team

**Sharon Mates, PhD,** Founder, Chairman, President & Chief Executive Officer

**Robert Davis, PhD,** Senior Vice President, Chief Scientific Officer

**Suresh Durgam, MD,** Senior Vice President, Late Stage Clinical Development and Medical Affairs

**Michael I. Halstead,** Executive Vice President and General Counsel

**Larry Hineine,** Senior Vice President Finance & Chief Financial Officer

**Mark Neumann,** Executive Vice President & Chief Commercial Officer

**Juan Sanchez, MD,** Vice President, Corporate Communications and Investor Relations

**Andrew Satlin, MD,** Executive Vice President & Chief Medical Officer

**Kimberly Vanover, PhD,** Senior Vice President, Early Stage Clinical Development and Translational Medicine



# Key Financial Metrics

## KEY METRICS

Total Cash, Cash Equivalents, and Investments*	\$312.8 million
Total Debt*	\$0.0 million
Common Shares Outstanding*	55,131,125
Stock Options/Restricted Stock Units Outstanding*	7,577,832

\*As of March 31, 2019 (unaudited).

