# **Corporate Presentation**





#### 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 December 27, 2019
    - For the treatment of bipolar depression
  - Leader in the field of PDE1 inhibitors
    - Parkinson's disease
    - Heart failure
- Well-capitalized
  - \$285.3 million in cash, cash equivalents and investment securities at 6/30/2019





# **ITCI Therapeutic Pipeline**



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



# Schizophrenia Is a Common Disabling Neuropsychiatric Disease





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

2.4 million adults in the United States have schizophrenia<sup>2</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>3</sup>

1. National Alliance on Mental Illness. https://www.nami.org/Learn-More/Mental-Health-Conditions/Schizophrenia. Accessed Aug 6, 2019.

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

<sup>2.</sup> National Institutes of Health. https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=67. Accessed Aug 6, 2019.

# Lumateperone Is Designed to Address Unmet Needs in Schizophrenia

- Available treatment options fail to adequately control the broad spectrum of symptoms
- Antipsychotics are associated with a host of side effects
  - Weight gain and metabolic disturbances
  - Hyperprolactinemia
  - Movement disorders
- These side effects drive poor medication adherence, thus reducing effectiveness of therapy
- Side effects also contribute to excessive premature mortality



### Lumateperone Schizophrenia Program Overview

- Lumateperone 42 mg (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
- Statistically significant safety and tolerability benefits for lumateperone over risperidone
- Once daily oral dosing with no need for titration to 42 mg
- NDA under FDA review, PDUFA target action date December 27, 2019



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

#### Lumateperone 42 mg Met Primary Endpoint in 2 Positive Large Schizophrenia Studies

<u>ITI-007-005</u>

ITI-007-301



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



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

- The study evaluated the safety of lumateperone 42 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, endocrine parameters over 6 weeks of treatment with lumateperone
- When switched back to SOC medication, worsened again



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

## Lumateperone Exhibited a Favorable Cardiometabolic Profile with Long-Term



Other metabolic parameters showed minimal to no changes with long-term treatment LDL, low-density lipoprotein; SOC, standard of care.



# Long-Term Safety Study Demonstrated Weight Decreased on Lumateperone

Change in Body Weight



| Patients With Significant Change in<br>Weight (≥7%) at Any Time During the<br>Study |     |  |
|---|-----|--|
| Weight decrease   | 24% |  |
| Weight increase   | 8%  |  |

Intra-Cellular

\**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 Long-Term Safety Study in Patients with Co-morbid Depression 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 (≥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









# **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 adult Americans<sup>2</sup>
  - Bipolar depression (BPD) is the predominant presentation
  - Depressive episodes are longer and recur more often than manic/hypomanic episodes
- Unmet need
  - Few approved treatments available for bipolar depression
  - Only one treatment approved for Bipolar II patients with depressive episodes
  - Safety and tolerability trade-off 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. Accessed Aug 6, 2019.
- 2. Depression and Bipolar Support Alliance. <u>https://www.dbsalliance.org/education/bipolar-disorder/bipolar-disorder-statistics/</u>. Accessed Aug 6, 2019.



### Lumateperone Bipolar Depression Program Overview

- Study 404 met its primary endpoint for improvement on MADRS compared with placebo (p<0.0001; effect size = 0.56)</li>
- Study 404 also met its key secondary objective (CGI-BP-S; p<0.001; effect size = 0.46)
- Study 404 benefits were statistically significant in both Bipolar I and Bipolar II patients
- In Study 401, lumateperone did not separate from placebo. A high placebo response was observed in the trial.
- Favorable safety and tolerability profile observed in both trials, consistent with prior lumateperone trials.

#### 3 Large Randomized, Double-Blind Trials

Primary outcome measure: change from baseline on Montgomery-Åsberg Depression Rating Scale (MADRS) Total Score

#### ITI-007-404 - Global

*Monotherapy 6-week treatment period N=381* 

- luma 42 mg or

- Placebo

#### ITI-007-401 – US-only

*Monotherapy 6-week treatment period N=554* 

- luma (42 mg or 28 mg) or

- Placebo

#### ITI-007-402-ongoing

*Adjunctive 6-week treatment period N=696* 

luma (42 mg or 28 mg) or
Placebo



### Study 404: Lumateperone Met Primary Endpoint - Change From Baseline to Day 43 in MADRS Total Score

Change From Baseline to Day 43 in MADRS Total Score

| Treatment Group             | Baseline<br>Mean | LS Mean<br>Change at<br>Day 43 | p value | Effect Size |
|-----------------------------|------------------|--------------------------------|---------|-------------|
| Lumateperone 42 mg<br>N=188 | 30.7             | -16.7                          | <.0001  | -0.56       |
| Placebo<br>N=188            | 30.2             | -12.1                          | -       | -           |

- Lumateperone 42 mg also met key secondary endpoint: the CGI-BP-S Total Score (p<0.001; effect size = 0.46)
  - CGI component that specifically assesses depression (CGI-BP-S Depression Score; p<0.001; effect size = 0.50)
- Statistically significant benefits on responder rates and remission rates, demonstrating the clinical meaningfulness of the primary outcome.
- Statistically significant improvement versus placebo on the MADRS in Bipolar I and Bipolar II
- Study 404 benefits were statistically significant in both subgroups : US and Ex-US



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

- PDEI 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 inhibitor molecule, is being developed for the treatment of Parkinson's disease and heart failure







- Over 2.2 million patients in the US and Europe<sup>1,2</sup>
- Unmet need

2. European Parkinson's Disease Association.

tion - epda.pdf. Accessed Aug 6, 2019.

- 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 Aug 6, 2019.





- A Phase 1/2, placebo-controlled, multiple ascending dose cohort study in patients with mild to moderate PD maintained on stable (concomitant) PD medication
- 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 Part III and Part IV of the MDS-UPDRS
  - Reduced dyskinesia symptoms seen in UDysRS and increase in "ON" time without dyskinesia (Hauser Patient Motor Diary)
  - 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>
- 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  $A_{\rm 2B}$  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
  - Study evaluates contractility and pharmacodynamic parameters
  - Clinical conduct for the second cohort, 30 mg, is ongoing; no safety concerns have been 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

- Acts as a partial agonist at mu opioid receptors (MOP) receptors and has high affinity at 5-HT2A, and D1 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

 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 Aug 6, 2019.

2. U.S. Department of Health and Human Services. <u>https://www.hhs.gov/opioids/</u> . Accessed Aug 6, 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 Hineline            | Senior Vice President Finance & Chief Financial Officer                            |
| Mark Neumann              | Executive Vice President & Chief Commercial Officer                                |
| Michael Olchaskey, PharmD | Senior Vice President, Head of Regulatory Affairs                                  |
| 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*                   | \$285.3 million |  |
| Total Debt <sup>*</sup>  | \$0.0 million   |  |
| Common Shares Outstanding*                                       | 55,186,745      |  |
| Stock Options/Restricted Stock Units<br>Outstanding <sup>*</sup> | 7,971,604       |  |





