Caplyta® (lumateperone) – New drug approval

- On December 23, 2019, Intra-Cellular Therapies' announced the FDA approval of Caplyta (lumateperone), an atypical antipsychotic indicated for the treatment of schizophrenia in adults.

- Schizophrenia is a psychiatric condition that involves chronic and recurrent psychosis and is commonly associated with impairments in social and occupational functioning.
  - Schizophrenia is characterized by positive symptoms (hallucinations, delusions, and disorganized speech) and negative symptoms (flat affect, poverty of speech, impairments in cognition, attention, memory and executive functions).
  - Schizophrenia occurs in approximately 1% of the US population.
  - First-line treatment for schizophrenia includes antipsychotics.

- The exact mechanism of Caplyta is unknown; however efficacy is thought to be mediated through a combination of antagonist activity at central serotonin 5-HT_{2a} receptors and postsynaptic antagonist activity at central dopamine D_2 receptors.

- The efficacy of Caplyta was established in two, four-week, randomized, double-blind, placebo-controlled, multi-center studies in adults with a diagnosis of schizophrenia. In both trials the primary efficacy measure was change the Positive and Negative Syndrome Scale (PANSS) total score at Day 28. The PANSS measures symptoms of schizophrenia.
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  - In **Study 1**, 335 patients with randomly assigned to receive Caplyta 42 mg, Caplyta 84 mg, an active comparator, or placebo once daily. After 28 days of treatment, patients treated with Caplyta 42 mg demonstrated a significantly greater mean change in PANNS compared to placebo (-13.2 points vs -7.4 points, respectively). When compared to placebo, the Caplyta 84 mg group was not statistically different.
  - In **Study 2**, 450 patients were randomly assigned to receive Caplyta 28 mg, Caplyta 42 mg, or placebo once daily. After 28 days of treatment, patients treated with Caplyta 42 mg demonstrated a significantly greater mean change in PANNS compared to placebo (-14.5 points vs -10.3 points, respectively). When compared to placebo, the Caplyta 28 mg group was not statistically different.

- Caplyta carries a boxed warning; Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Caplyta is not approved for the treatment of patients with dementia-related psychosis.

- Caplyta is contraindicated in patients with known hypersensitivity to lumateperone or any components of Caplyta.

- Warnings and precautions for Caplyta include increased incidence of cerebrovascular adverse reactions (e.g., stroke and transient ischemic attack) in elderly patients with dementia-related psychosis; potential for neuroleptic malignant syndrome; tardive dyskinesia; metabolic changes; leukopenia, neutropenia, and agranulocytosis; orthostatic hypotension and syncope; falls; seizures; potential for cognitive and motor impairment; body temperature dysregulation; and dysphagia.

- The most common adverse reactions (≥ 5% and greater than twice placebo) with Caplyta use were somnolence/sedation and dry mouth.

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- The recommended dose of Caplyta is 42 mg administered orally once daily with food. Dose titration is not required.

- Intra-Cellular Therapies plans to launch Caplyta in the first quarter of 2020. Pricing information will be disclosed closer to launch. Caplyta will be available as a 42 mg oral capsule.