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ACP-204 Clinical Development Program in Lewy Body Dementia Psychosis

This letter is provided in response to your specific request for information regarding the ACP-204 clinical development program in Lewy body dementia (LBD) psychosis. ACP-204 is an investigational agent, and its safety and efficacy for the treatment of hallucinations and delusions associated with LBD psychosis have not been established and approved by the FDA.

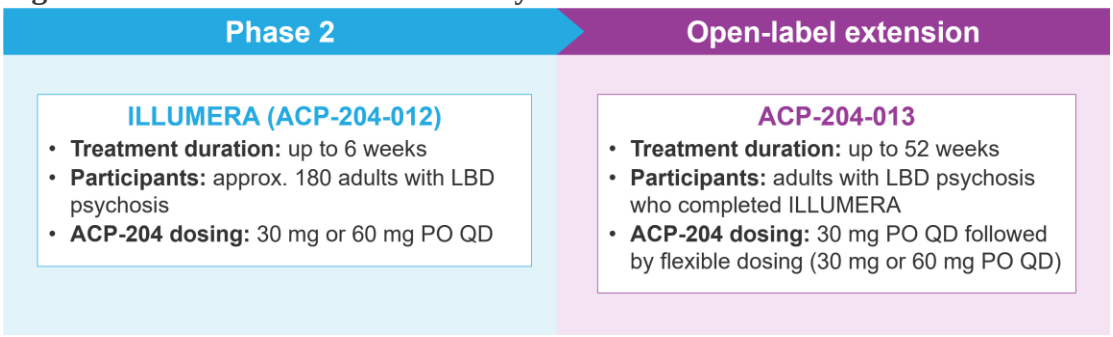
Summary

- The efficacy and safety of ACP-204 (30 mg and 60 mg, once daily [QD]) is being investigated in adults with hallucinations and delusions associated with LBD psychosis in the Phase 2 **ILLUMERA** study (ACP-204-012).[1,2]
    - The primary endpoint is the change from baseline in Scale for Assessment of Positive Symptoms–LBD psychosis (SAPS-LBDP) total score at Week 6.[2]
- Participants completing ILLUMERA will be eligible to enroll in an open-label extension (OLE) study, **ACP-204-013**, that will evaluate the safety and tolerability of long-term ACP-204 treatment in participants with LBD psychosis for up to 52 weeks.[3]

Clinical Studies in LBD Psychosis

The efficacy and safety of ACP-204 is being investigated in participants with hallucinations and delusions associated with LBD psychosis in a 6-week Phase 2 study and a long-term OLE study (**Figure 1**).[1,3]

Figure 1. ACP-204 Studies in LBD Psychosis[1,3]



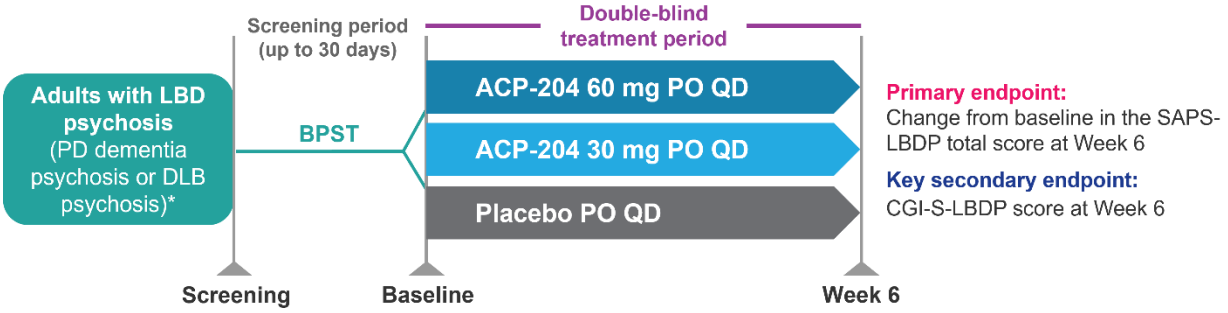
Abbreviations: LBD=Lewy body dementia; PO=orally; QD=once daily.

ILLUMERA (ACP-204-012)

ILLUMERA is a multicenter, randomized, double-blind, placebo-controlled, parallel-group, Phase 2 study in participants with LBD psychosis (i.e. either PD dementia psychosis or DLB psychosis). An estimated 180 participants will be randomized to one of 3 parallel arms, i.e., ACP-204 at one of 2 dose levels (30 or 60 mg) or placebo, for a double-blind treatment period of up to 6 weeks (**Figure 2**). Randomization will be stratified by diagnosis of PD dementia psychosis (50% cap) or DLB psychosis. The primary endpoint measure, SAPS-LBDP total score,

includes the same 9 of the 20 hallucinations and delusions items in the Scale for Assessment of Positive Symptoms Hallucinations and Delusions domains (SAPS-H+D) as the PD-adapted Scale for Assessment of Positive Symptoms (SAPS-PD). The key secondary endpoint measure, the Clinical Global Impression-Severity (CGI-S)-LBDP scale, is the CGI-S scale applied in the LBD psychosis context, in which hallucinations and delusions are the symptoms of interest.[2]

Figure 2. ILLUMERA Study Design[2]



**Randomization stratified by diagnosis of PD dementia psychosis (50% cap) or DLB psychosis (no cap).*
Abbreviations: BPST=brief psychosocial therapy; CGI-S-LBDP=Clinical Global Impression–Severity in the LBD psychosis context; DLB=dementia with Lewy bodies; LBD=Lewy body dementia; PD=Parkinson's disease; PO=orally; QD=once daily; SAPS-LBDP=Scale for Assessment of Positive Symptoms in the LBD psychosis context.

There will be a screening period of up to 30 days, during which the designated study partner/caregiver will be given instructions on engaging in a structured psychosocial interaction with the participant (brief psychosocial therapy). After completing the 6-week double-blind treatment period, participants who do not enroll in the OLE study will undergo a 30-day safety follow-up period. An additional mortality follow-up will be conducted for participants who discontinue prematurely from the study 30 days after the participant's intended day of last dose of study drug.[2] Selected inclusion and exclusion criteria for ILLUMERA are shown in **Table 1**.

Table 1. ILLUMERA Selected Inclusion and Exclusion Criteria[2]

Selected inclusion criteria

• Male or female participants, ≥55 and <85 years of age, living in the community or in an institutionalized setting
• Meets either the clinical criteria for PD with dementia (as defined by the MDS Task Force) or revised clinical criteria for probable DLB (Fourth Consensus report of the DLB Consortium)
• Meets the revised criteria for psychosis in major or mild neurocognitive disorder established by the IPA
• MMSE score ≥6 and ≤28 at screening and baseline
• Had psychotic symptoms for ≥2 months prior to screening visit
• Has the following scores at screening and baseline:
  ○ SAPS Hallucinations or Delusions global item (H7 or D13) score ≥3 AND a score ≥3 on at least one other non-global item using the SAPS-LBDP
  ○ CGI-S-LBDP score ≥4
• Has a prior MRI or CT scan of the brain that is consistent with the diagnosis of LBD
• Must be on a stable dose of cholinesterase inhibitor, memantine, and/or dopaminergic medications

Selected exclusion criteria
• In hospice and receiving end-of-life palliative care, or has become bedridden • Requires ongoing skilled nursing or medical care of IV lines or surgical openings to the wind-pipe or bladder • Has psychotic symptoms that are primarily attributable to delirium, substance abuse, or a medical or psychiatric condition other than dementia

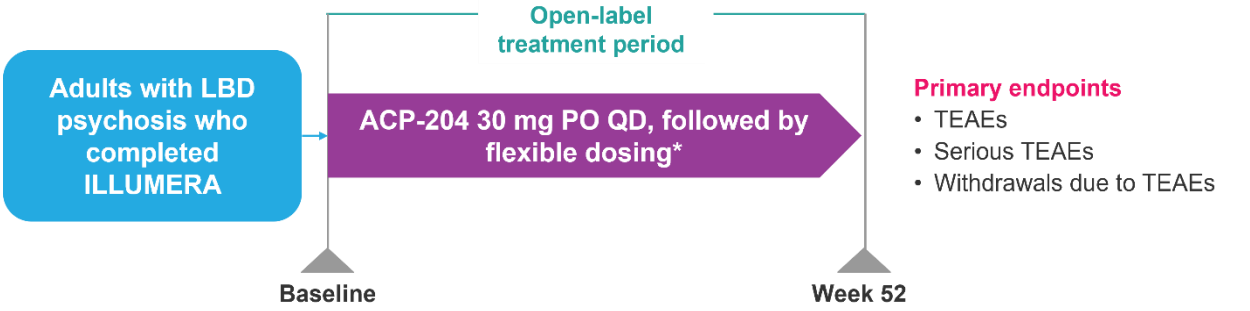
- Has evidence of a non-neurologic medical comorbidity or medication use that could substantially impair cognition
- Has a known history of cerebral amyloid angiopathy, epilepsy, central nervous system neoplasm, or unexplained syncope
- Atrial fibrillation
- Has a known personal or family history or symptoms of long QT syndrome

Abbreviations: CGI-S-LBDP=Clinical Global Impression-Severity in the LBDP context; CT=computed tomography; DLB=dementia with Lewy bodies; IPA=International Psychogeriatrics Association; LBD=Lewy body dementia; LBDP=Lewy body dementia psychosis; MDS=Movement Disorder Society; MMSE=Mini-Mental State Examination; MRI=magnetic resonance imaging; PD=Parkinson's disease; SAPS=Scale for Assessment of Positive Symptoms; SAPS-LBDP=LBDP-adapted Scale for the Assessment of Positive Symptoms.

ACP-204-013

This is a 52-week, OLE study enrolling participants who complete the Phase 2 ILLUMERA study (**Figure 3**). The primary objective is to evaluate the safety and tolerability of long-term ACP-204 treatment in participants with LBD psychosis.[3]

Figure 3. Study Design for ACP-204-013[3]



**After the initial ACP-204 dose of 30 mg on the day after the baseline visit, the ACP-204 dose may be adjusted first up for suboptimal efficacy or later down for tolerability concerns, once or more than once, to 30 mg or 60 mg administered QD.*
Abbreviations: LBD=Lewy body dementia; PO=orally; QD=once daily; TEAE=treatment-emergent adverse event.

All eligible rollover participants from ILLUMERA will begin ACP-204 30 mg QD dosing on the day after the end-of-treatment visit for the antecedent study, which serves also as the baseline visit for this study, ACP-204-013. After the initial ACP-204 dose of 30 mg on the day after the baseline visit, the ACP-204 dose is flexible, and may be adjusted first up for suboptimal efficacy or later down for tolerability concerns, once or more than once, to 30 mg or 60 mg administered QD.[3]

References

1. National Institutes of Health. Multicenter, randomized, 6-week, double-blind, placebo-controlled, parallel-group, Phase 2 study in subjects with LBDP. [Link].
2. Acadia Pharmaceuticals Inc. Data on File. ACP-204-012 Protocol. 2025.
3. Acadia Pharmaceuticals Inc. Data on File. ACP-204-013 Protocol. 2025.