ACADIA® Pharmaceuticals

Steve Davis, CEO

37th Annual
J.P. Morgan
Healthcare Conference

JANUARY 9, 2019

# Forward-Looking Statement

This presentation contains forward-looking statements. These statements relate to future events and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Each of these statements is based only on current information, assumptions and expectations that are inherently subject to change and involve a number of risks and uncertainties. Forward-looking statements include, but are not limited to, statements about (i) plans for, including timing and progress of commercialization of, NUPLAZID® or for the clinical development of our product candidates, including pimavanserin and trofinetide; (ii) benefits to be derived from and efficacy of our product candidates, including the use of pimavanserin in dementia-related psychosis, schizophrenia, depression or other neurological or psychiatric indications, potential advantages of NUPLAZID versus existing antipsychotics or antidepressants, and expansion opportunities for NUPLAZID; (iii) estimates regarding the prevalence of PD, PD Psychosis, dementia-related psychosis, schizophrenia or depression and the potential use of trofinetide in Rett syndrome; (iv) potential market for any of our products, including NUPLAZID and trofinetide; and (v) our estimates regarding our future financial performance, cash position or capital requirements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions (including the negative thereof) intended to identify forward-looking statements. Given the risks and uncertainties, you should not place undue reliance on these forward-looking statements. For a discussion of the risks and other factors that may cause our actual results, performance or achievements to differ, please refer to our annual report on Form 10-K for the year ended December 31, 2017 as well as our subsequent filings with the SEC. The forward-looking statements contained herein are made as of the date hereof, and we undertake no obligation to update them for future events.





ACADIA® Pharmaceuticals

Improving Lives




# Our Vision

*Become the leading pharmaceutical company dedicated to the advancement of innovative medicines that improve the lives of patients with CNS disorders*

# ACADIA Today

- NUPLAZID® - the first and only FDA approved treatment for hallucinations and delusions associated with Parkinson's disease psychosis
- Highly innovative, late-stage clinical pipeline
  - 5 late-stage clinical programs addressing significant unmet needs in CNS
  - Breakthrough therapy designation in dementia-related psychosis (DRP) for pimavanserin
  - Fast track status and Orphan Drug designation in Rett syndrome for trofinetide



NUPLAZID is approved in the U.S. for the hallucinations and delusions associated with Parkinson's disease psychosis
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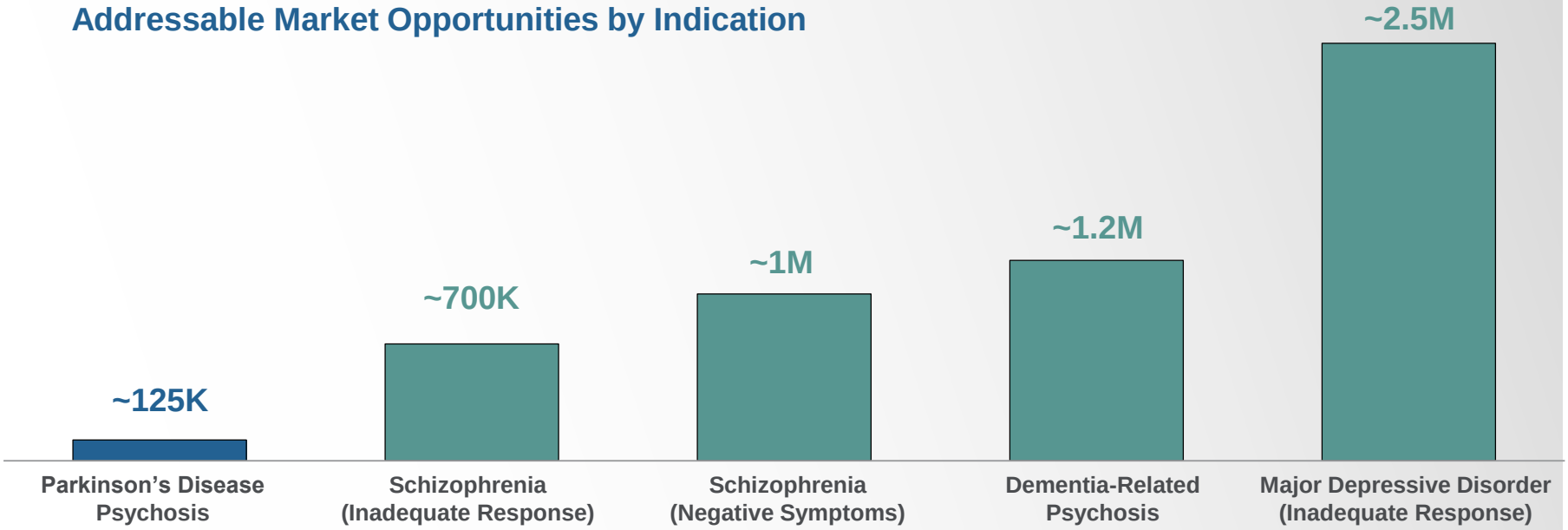
# NUPLAZID®/Pimavanserin: Significant Opportunities in Addition to PDP

## Addressable Market Opportunities by Indication




**PDP:** ~125,000 patients currently receive some form of treatment for PDP; ACADIA market research.
**Schizophrenia (Inadequate response):** ~1% of adults in the U.S. have schizophrenia[1], ~30% inadequately respond to current therapies[2]
**Schizophrenia (Negative symptoms):** ~1% of adults in the U.S. have schizophrenia[1], studies suggest that ~40-50% of patients with schizophrenia experience prominent negative symptoms.
**DRP:** ~8 million patients in the U.S. have dementia, ~2.4 million have dementia-related psychosis; ~1.2 million are diagnosed with dementia-related psychosis[3]
**MDD:** ~2.5 million patients currently receive adjunctive therapy for MDD[4]



[1]According to National Institute of Mental Health; [2]According to American Psychiatric Association; [3]2017 Alzheimer's Disease Facts and Figures and ACADIA market research [4] IMS NSP, NPA, NDTI MAT-24 month data through Aug-2017; PLOS One, Characterization of Treatment Resistant Depression Episodes in a Cohort of Patients from a US Commercial Claims Database, Oct 2013, Vol 8, Issue 10.
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# 3 Strategic Pillars to Achieving our Vision

## Grow…

**…NUPLAZID® as the only approved treatment and standard of care for patients with Parkinson's disease psychosis**

## Leverage…

**…the potential of pimavanserin by expanding to additional indications with significant unmet need**

## Expand…

**…our pipeline through focused business development in CNS disorders with high unmet need**



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# Recent Highlights of Executing on our Strategy

## ADVANCED NUPLAZID® AS THE STANDARD OF CARE IN PARKINSON'S DISEASE PSYCHOSIS

- Launched 34 mg capsule in 3Q18
- Launched branded DTC campaign in 4Q18
- Significant opportunity to help more patients with PDP

## PROGRESSED LATE-STAGE CLINICAL PIPELINE

- **Major Depressive Disorder (MDD):** Positive results in Phase 2 CLARITY study; Phase 3 to initiate 1H19
- **Dementia-Related Psychosis (DRP):** Phase 3 HARMONY study progressing
- **Schizophrenia:** Phase 3 ENHANCE study in Inadequate Response and Phase 2 ADVANCE study in Negative Symptoms progressing

## EXPANDED LATE STAGE PIPELINE

- **Acquired North American Rights to Trofinetide:** Phase 3 study to initiate in Rett syndrome in 2H19



NUPLAZID is approved in the U.S. for the hallucinations and delusions associated with Parkinson's disease psychosis



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# Grow…

# NUPLAZID®: The First and Only Approved Treatment for PDP

## NUPLAZID is a selective serotonin inverse agonist/antagonist, or SSIA

- Preferentially targets 5-$HT_{2A}$ receptors
- Non-dopaminergic antipsychotic
- Demonstrated significant efficacy in reducing hallucinations and delusions of PDP
- 74% of patients experienced improvement in pivotal clinical study

## Well-tolerated in clinical studies in PDP patients

- No impairment of motor symptoms
- No increased sedation
- No weight gain
- No orthostatic hypotension
- No blood disorders


ONCE-DAILY
NUPLAZID®
(pimavanserin) 34mg capsules



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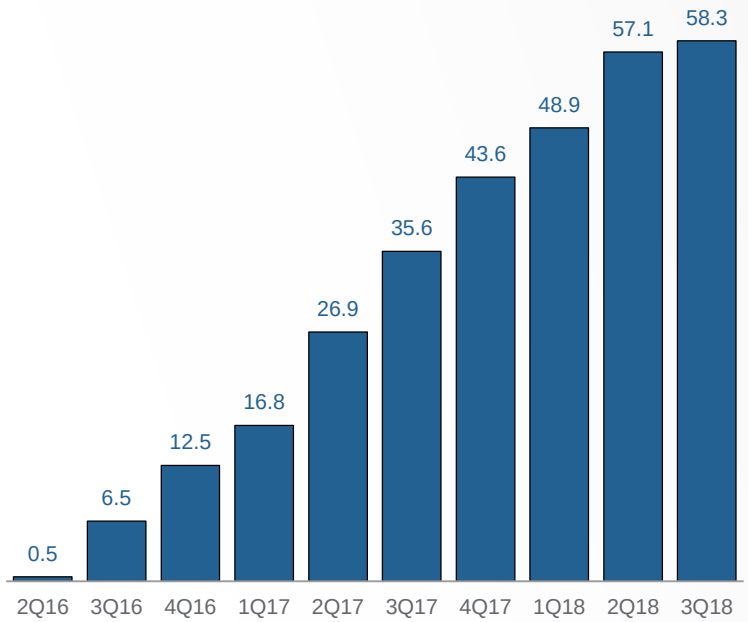
# NUPLAZID®: Significant Commercial Opportunity Ahead in PDP

## NUPLAZID Net Sales ($M)




*Company converted to sell-in method from sell-through method in 2Q 2017. All revenues shown above are on a sell-in basis for consistency of presentation.*

**Revenue:**

- 2018 NUPLAZID Revenue Guidance: $220 - $225M
- 3Q18 Revenue of $58.3M; +64% YoY growth

**Market Opportunity:**

- ~1 million people in the U.S. have Parkinson's disease
- ~50% will experience psychosis over the course of their disease
- ~125K patients currently treated for PDP*
- One study** showed over a six year period:
  - 24% of all hospitalizations for PD patients were for psychosis alone
  - Additional 25% of hospitalizations for motor and psychiatric complications



*ACADIA market research; **Klein C, Prokhorov T, Miniovitz A, et al. Admission of Parkinsonian patients to a neurological ward in a community hospital. *J Neural Transm (Vienna).* 2009;116(11):1509-1512
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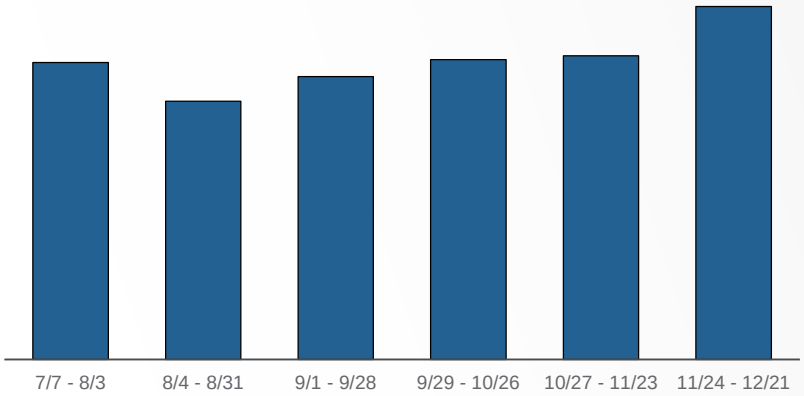
# NUPLAZID® Growth Trends by Channel

## Specialty Pharmacy

***New Patient Starts***

**(Weekly Avg)**

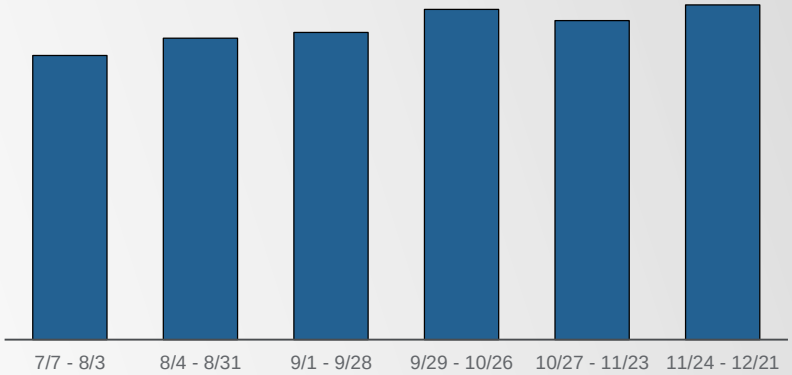



**Weekly average new patient starts increasing**

## Long-Term Care (Specialty Distribution*)

***Total Bottles – Including Refills***

**(Weekly Avg)**




**Continued growth in long-term care bottles**



*Long-term care represents ~2/3 of our specialty distribution business



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# NUPLAZID® Branded DTC Campaign: Raising Awareness Among Patients and Caregivers


**NUPLAZID is the Only FDA Approved Medicine Proven to Reduce the Frequency and/or Severity of Hallucinations and Delusions Associated with Parkinson's Disease Psychosis**



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# Leverage…

# Significant Opportunities with Late-Stage Pipeline

| COMPOUND/ PROGRAM | INDICATION | IND-TRACK | PHASE 1 | PHASE 2 | PHASE 3 | MARKETED |
|---|---|---|---|---|---|---|
| NUPLAZID® (pimavanserin)* | Hallucinations and Delusions Associated with PD Psychosis | | | | | |
| Pimavanserin | Dementia-Related Psychosis | | | | | |
| Pimavanserin | Schizophrenia Inadequate Response | | | | | |
| Pimavanserin | Major Depressive Disorder Inadequate Response | | | | | |
| Pimavanserin | Schizophrenia Negative Symptoms | | | | | |
| Trofinetide** | Rett Syndrome | | | | | |



*NUPLAZID is approved in the U.S; **ACADIA has an exclusive license to develop and commercialize trofinetide in North America from Neuren Pharmaceuticals.
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# Dementia-Related Psychosis (DRP)

**HIGH UNMET NEED**

***No FDA approved treatment***

**~1.2M**

**People in the U.S. are diagnosed with DRP***

**Serious consequences:**

- Repeated hospital stays
- Earlier progression to nursing home
- More rapid progression of dementia
- Increased risk of morbidity and mortality

**Current antipsychotics used off-label accelerate cognitive decline – equivalent to about one year of disease progression – and carry significant side effects****



*2017 Alzheimer's Disease Facts and Figures and ACADIA market research

**Schneider LS, Tariot PN, Dagerman KS, et al, CATIE-AD Study Group. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. *N Engl J Med 2006*; 355: 1525–38

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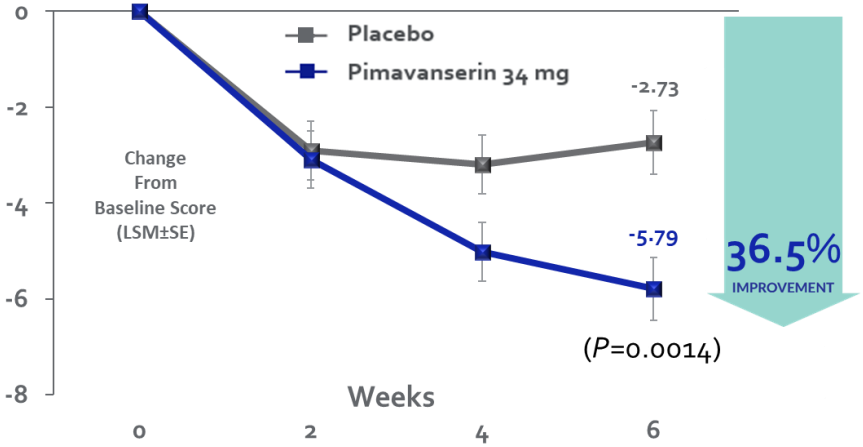
# Clinical Efficacy in Parkinson's Disease Psychosis and Alzheimer's Disease Psychosis Studies

## Parkinson's Disease Psychosis, Phase 3 020 Study*

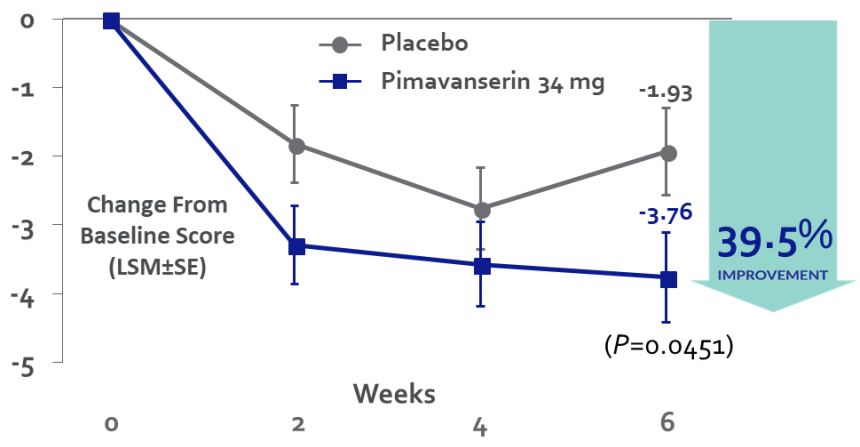
**NUPLAZID 34 mg showed a 36.5% improvement in primary endpoint (Change in SAPS-PD score from baseline to Day 43) versus 18.5% for placebo**




**Note:** ~25% of subjects enrolled in this 199 patient study met criteria for dementia with MMSE score <25. In this dementia subgroup, for the primary efficacy analysis at Day 43, a treatment difference of 5.71 points (*p=0.0018*) was observed with an effect size of 0.99.

## Alzheimer's Disease Psychosis, Phase 2 019 Study**

**Pimavanserin 34 mg showed a 39.5% improvement in primary endpoint (Change from baseline to Day 43 in the NPI-NH psychosis subscale) versus 19% for placebo**




LSM: least-squares mean; SE: standard error

*NUPLAZID Prescribing Information; Cummings J, et al. Lancet. 2014;383:533-540.; **Ballard C, et al. Lancet. 2018;17:213-222.

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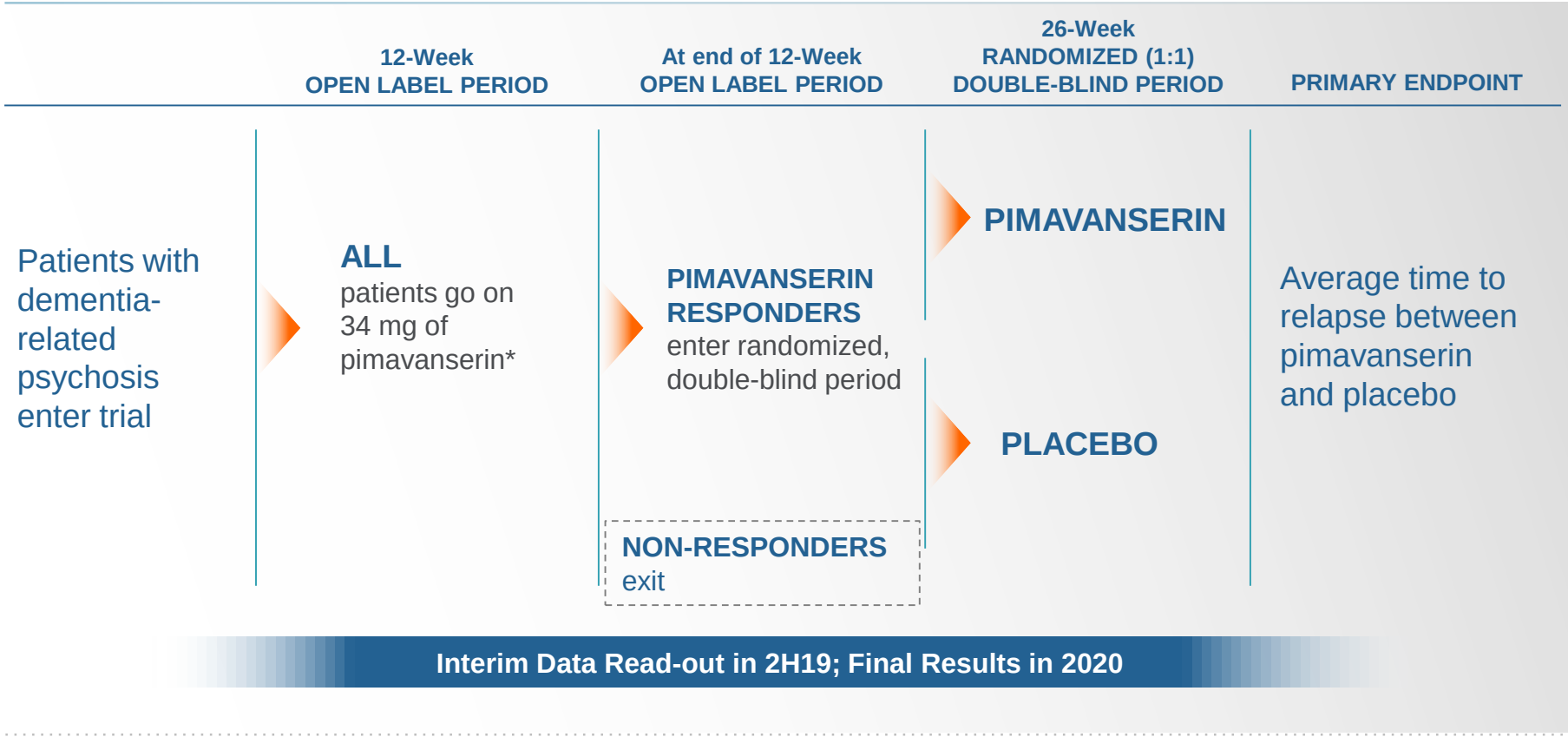
# Phase 3 HARMONY Relapse Prevention Study Design






*Patients are able to reduce dose from 34 mg to 20 mg of pimavanserin in the first 4 weeks of open label period.



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# Major Depressive Disorder (MDD) – Inadequate Response

## HIGH UNMET NEED

Majority of patients with MDD do not respond to initial antidepressant therapy

**~2.5M** in U.S. treated with adjunctive therapy*

**Based on market research, there is significant need for:**

- Greater efficacy

- Faster speed of onset
- Treatment without sexual dysfunction
- Treatment without weight gain
- Treatment without daytime sleepiness
- Treatment without negative impact on motor function including rare but serious tardive dyskinesia

## PHASE 2 CLARITY RESULTS

Pimavanserin was evaluated as an adjunctive treatment to SSRI/SNRI for treating MDD in a two-stage sequential parallel comparison design (SPCD)

- ✓ Primary endpoint achieved – depression (HAMD-17**) *p=0.039*
- ✓ Key secondary endpoint achieved – disability (SDS**) *p=0.004*
- ✓ Positive results also observed on 7 additional pre-specified secondary endpoints (*p<0.05*)***

- ✓ Early efficacy (week 1) and sustained efficacy (week 10)
- ✓ Improvement in sexual function
- ✓ No meaningful weight gain
- ✓ Reduction in daytime sleepiness
- ✓ No motor function side effects observed

*Pre-specified efficacy analysis: Weighted average of treatment difference from Stage 1 and Stage 2 of study*



*IMS NSP, NPA, NDTI MAT-24 month data through Aug-2017; PLOS One, Characterization of Treatment Resistant Depression Episodes in a Cohort of Patients from a US Commercial Claims Database, Oct 2013, Vol 8, Issue 10.
**HAMD-17: 17-item Hamilton Depression Rating Scale; SDS = Sheehan Disability Scale; *** Additional secondary endpoints are nominal p-values.
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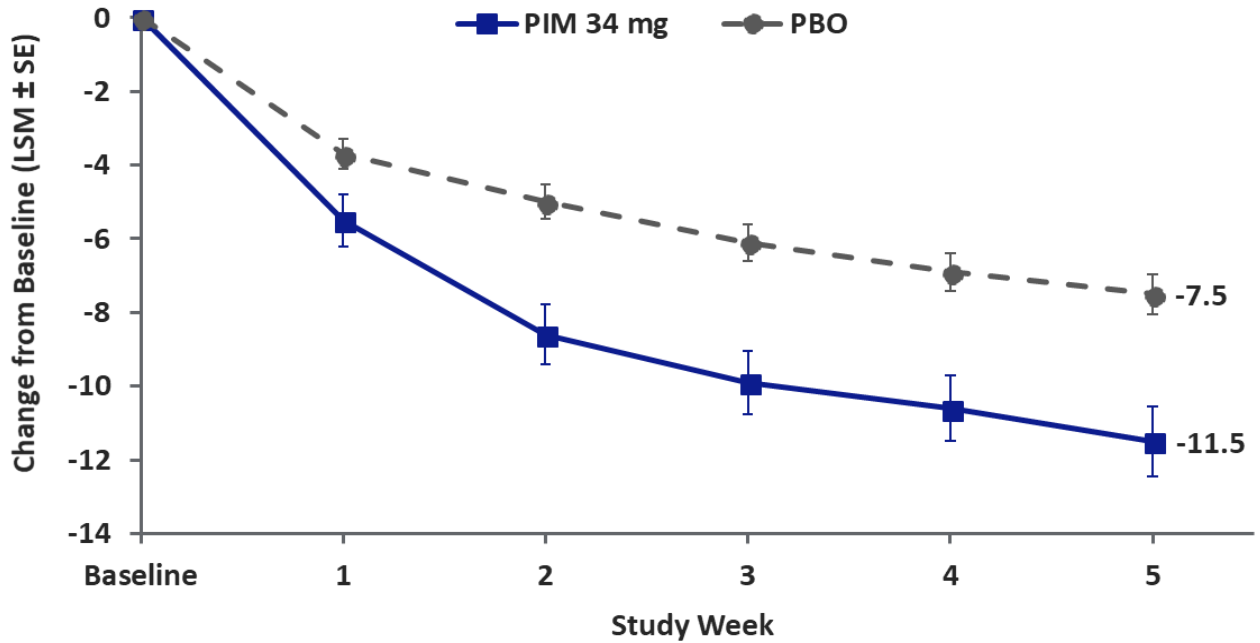
# CLARITY: Pimavanserin Significantly Improved Patients' HAMD-17 Total Score vs. Placebo in Stage 1




| No. of subjects | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 152 | 148 | 141 | 135 | 131 | 127 |
| PIM | 51 | 49 | 48 | 45 | 44 | 45 |
| *p-value* | | *0.0365* | *0.0003* | *0.0002* | *0.0004* | *0.0003* |
| **Effect Size** | | | | | | 0.626 |

Note: Weekly p-values (except week 5) are nominal

**HAMD-17 at Week 5**
***p-value = 0.0003***
***Effect Size = 0.626***

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# Next Steps in MDD

1 **Plan to meet with the FDA in early 2019**

2 **Given robust positive results, we believe the CLARITY study can serve as one of two pivotal trials required for sNDA submission**

3 **Initiate a Phase 3 Program in 1H19**

Plan to initiate two Phase 3 parallel design, placebo-controlled trials in adjunctive MDD on top of baseline SSRI/SNRI therapy




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# Schizophrenia – Inadequate Response

## HIGH UNMET NEED

### *No FDA-approved treatment*

**~1% of adults in the U.S. suffer from schizophrenia, a debilitating and lifelong condition***

**Current Treatment Response**


**Polypharmacy of currently available antipsychotics may lead to:**

- Increased side-effects
- Poor compliance
- Subsequent relapse

## CLINICAL PROGRAM

**Phase 2 data for pimavanserin in schizophrenia trial supports potential adjunctive treatment effect*****

**Phase 3 ENHANCE Study**

- **~380 patients** with inadequate response to current antipsychotic treatment for schizophrenia
- Randomized 1:1 (6 weeks) on pimavanserin + background therapy vs. placebo + background therapy
- Start daily dose of 20 mg pimavanserin at baseline; flexible dosing (10 mg, 20 mg, or 34 mg) between weeks 1 and 3
- **Primary endpoint –** change from baseline to week 6 on Positive and Negative Syndrome Scale (PANSS) total score
- **Data expected mid-2019**



*According to the National Institute of Mental Health; **According to the American Psychiatric Association
***Meltzer H, et al. *Schizophrenia Research.* 2012;141:144-152.
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# Schizophrenia – Negative Symptoms

## HIGH UNMET NEED

### *No FDA-approved treatment*

**~40% to 50%**

**Schizophrenia patients suffer prominent negative symptoms*:**

- Flat affect
- Loss of interest
- Emotional withdrawal
- Cognitive impairment

**Current antipsychotics target positive symptoms with minimal effect on negative symptoms**

Significant side-effect burden and poor compliance:

- Dramatic weight gain
- Highly sedating
- Cognitive impairment
- Blood disorders
- Motor symptoms

## CLINICAL PROGRAM

**Positive effect observed on PANSS negative symptom subscale when given in combination with low dose risperidone****

**Phase 2 ADVANCE Study**

- **~380 patients** with predominant negative symptoms of schizophrenia while on adequate treatment with an antipsychotic
- Randomized 1:1 for 26 weeks on pimavanserin + background therapy vs. placebo + background therapy
- Start daily dose of 20 mg pimavanserin at baseline; flexible dosing (10 mg, 20 mg, or 34 mg) between weeks 2 and 8
- **Primary endpoint –** change from baseline to week 26 in the Negative Symptom Assessment-16 (NSA-16) total score
- **Expect to complete enrollment in 2H19**



*Studies suggest ~40-50%; Patel et al. 2015, Haro et al., 2015, Bobes et al. 2010, and Chue and Lalonde, 2014.
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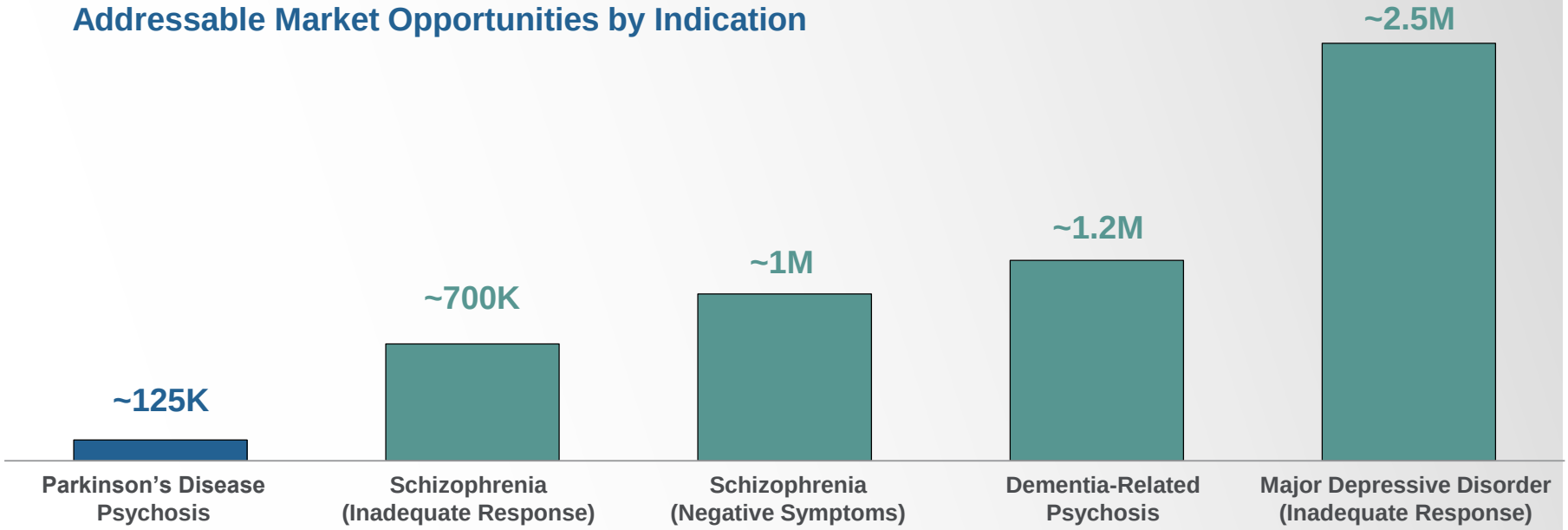


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# Expand…

# Disciplined Business Development Strategy

1. **Focus on CNS disorders with high unmet need**

2. **Leverage our highly talented CNS focused R&D organization, commercial organization and field team**

3. **Proven Execution:**
   **License agreement for North American rights for trofinetide completed 3Q18;**
   **Program advancing to Phase 3 initiation 2H19**




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# Rett Syndrome

**Rett syndrome is caused by mutations on the X chromosome on the MeCP2 gene:**

- **Debilitating neurologic rare disease**
- **6,000 to 9,000 patients in the U.S.***
- **No FDA-approved treatment**
- Primarily occurs in females causing problems in brain function with rapid decline between 6 and 18 months of age and can have the following symptoms:
  - Cognitive, sensory, emotional, motor impairment
  - Loss of independence
  - Loss of purposeful hand use
  - Loss of spoken communication



*According to the National Institutes of Health – National Institute of Neurological Disorders and Stroke



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# Trofinetide Clinical Program: Rett Syndrome

## Trofinetide

**Trofinetide is a novel synthetic analog of the amino-terminal tripeptide of IGF-1**

Designed to treat the core symptoms of Rett syndrome by reducing neuroinflammation and supporting synaptic function

**Phase 2 study:**

- Statistically significant improvements in **RSBQ*(*p-value = 0.042*)** and **CGI-I* (*p-value = 0.029*)** in girls 5 – 15 years of age

## PHASE 3 STUDY

- **Plan to initiate Phase 3 study in 2H19**
- **~180 girls** with Rett syndrome
- Double-blind, placebo-controlled

- **Co-primary endpoints:** RSBQ and CGI-I
- With positive results, potential to submit NDA in 2021

- **U.S. Fast Track Status**
- **Orphan Drug Designation in the U.S. and Europe for Rett syndrome**



*RSBQ = Rett Sydnrome Behaviour Questionnaire (caregiver assessment); CGI-I = Clinical Global Impression Scale-Improvement (physician assessment)



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# Clinical Milestones

| COMPOUND/ PROGRAM | INDICATION | MILESTONE | EXPECTED TIMING |
|---|---|---|---|
| Pimavanserin | Major Depressive Disorder Inadequate Response | End of Phase 2 meeting with FDA & commence Phase 3 program | 1H19 |
| Pimavanserin | Schizophrenia Inadequate Response | Phase 3 ENHANCE results | Mid-2019 |
| Pimavanserin | Dementia-Related Psychosis | Interim Phase 3 HARMONY results | 2H19 |
| | | Final Phase 3 HARMONY results | 2020 |
| Pimavanserin | Schizophrenia Negative Symptoms | Complete enrollment in Phase 2 ADVANCE study | 2H19 |
| Trofinetide | Rett Syndrome | Phase 3 trial initiation | 2H19 |




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# Committed to Executing on Our Key Priorities in 2019

## Continue to grow NUPLAZID®

- Execute on our commercial initiatives to grow NUPLAZID in PDP

## Leverage the potential of pimavanserin and advance trofinetide

- Five Phase 3 studies
- One Phase 2 study
- Two potential Phase 3 study read-outs

## Strong balance sheet to advance our pipeline and the potential to expand through business development



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*Committed to improving lives of patients with CNS disorders and their caregivers*