



# 3Q18 EARNINGS CALL

NOVEMBER 6, 2018



# Forward-Looking Statement

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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<sup>®</sup> 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.



# CEO Opening Remarks

Steve Davis  
President and CEO



# 3Q18 Earnings Call Agenda



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## INTRODUCTION

Elena Ridloff | Investor Relations and Interim Chief Financial Officer

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## CEO OPENING REMARKS

Steve Davis | President and Chief Executive Officer

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## R&D UPDATE

Serge Stankovic, M.D., M.S.P.H. | Head of Research & Development

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## COMMERCIAL UPDATE

Michael Yang | Chief Commercial Officer

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## FINANCE UPDATE

Elena Ridloff | Investor Relations and Interim Chief Financial Officer

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## CEO CLOSING REMARKS

Steve Davis | President and Chief Executive Officer

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## Q&A

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**ADVANCED  
NUPLAZID<sup>®</sup> AS  
STANDARD OF CARE  
IN PARKINSON'S  
DISEASE PSYCHOSIS\***

- ✓ **FDA issued a clear statement** reaffirming the positive benefit-risk profile of NUPLAZID on September 20<sup>th</sup>
- ✓ **Launched 34 mg capsule** in mid-August
- ✓ **3Q18 revenue of \$58.3 million**
  - ✓ YoY revenue growth of 64%

**ADVANCED  
LATE-STAGE  
CLINICAL PIPELINE**

- ✓ **Major Depressive Disorder (MDD):** Positive results announced from Phase 2 CLARITY study and plan to initiate Phase 3 program in 1H19
- ✓ **Ongoing Late-Stage Programs:** Phase 3 HARMONY for Dementia-Related Psychosis, Phase 3 ENHANCE in Schizophrenia Inadequate Response, and Phase 2 ADVANCE in Schizophrenia-Negative Symptoms
- ✓ **Acquired North American Rights to Trofinetide:** Expect to initiate Phase 3 study in Rett syndrome in 2H19

\*FDA approved for the hallucinations and delusions associated with Parkinson's disease psychosis  
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# Inadequate Response Major Depressive Disorder (MDD)

## High Unmet Need in MDD

~2.5M MDD people in U.S. treated with adjunctive therapy

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

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

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

## Phase 2 CLARITY Results

Based on primary and key secondary endpoints:

- ✓ Significant efficacy as assessed by primary and key secondary endpoints
- ✓ Early efficacy with separation at week 1
- ✓ Maintenance of effect through 10 weeks of treatment

Based on additional secondary endpoints and tolerability:

- ✓ Improvement in sexual function
- ✓ No meaningful weight gain
- ✓ Reduction in daytime sleepiness
- ✓ No impact on motor function



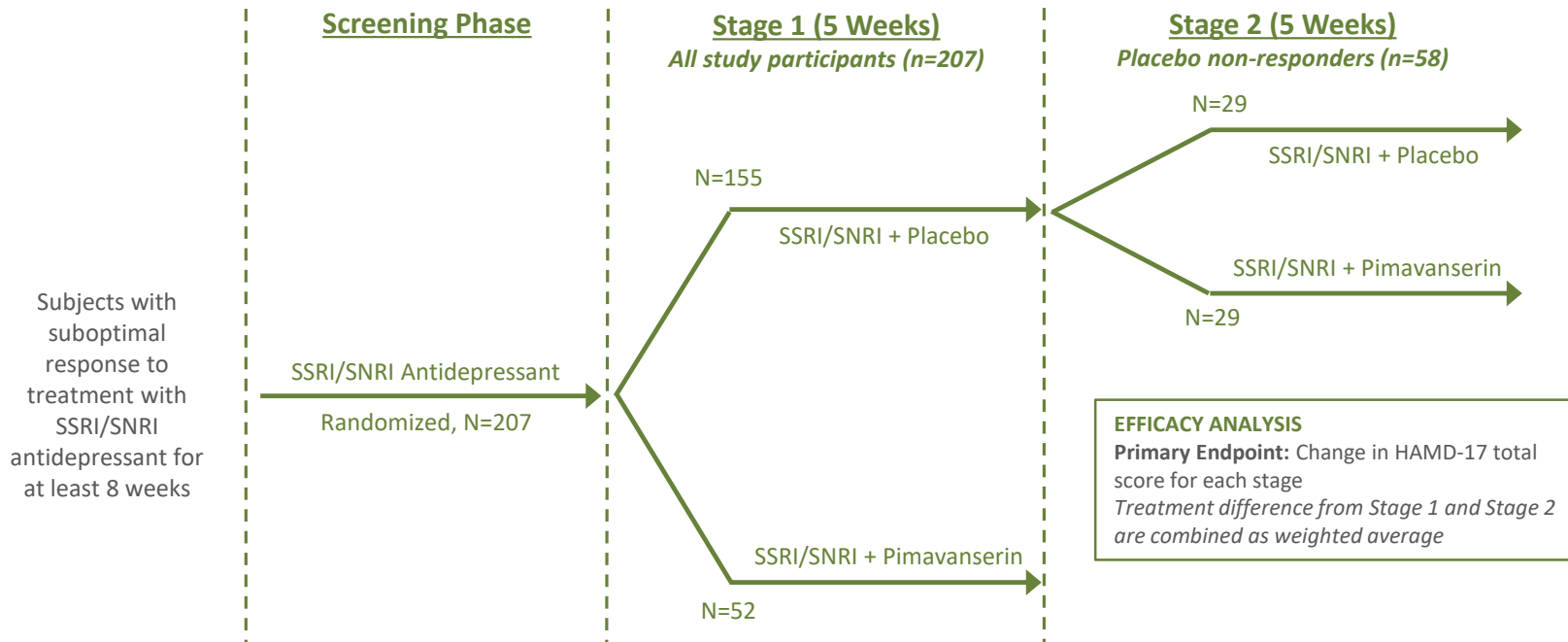


## R&D Update

Serge Stankovic, M.D., M.S.P.H.  
Head of Research and Development



# Phase 2 CLARITY Study Design



Note: For Stage 1, baseline is study week 0 and week 5 is study week 5. For Stage 2, baseline is study week 5 and week 5 is study week 10.

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# Positive Top-line Phase 2 CLARITY Results



	Overall	Stage 1 (5 weeks)		Stage 2 (5 weeks)	
		Pbo (n=152)	PIM (n=51)	Pbo to Pbo (n=29)	Pbo to PIM (n=29)
<b>Primary Endpoint:</b> HAMD-17 Total Score: LSM (SE) [Depression Scale]		-7.5 (0.55)	-11.5 (0.94)	-3.3 (0.94)	-2.8 (0.89)
<i>p-value</i>	<i>p=0.039</i>		<i>p=0.0003</i>		NS
Effect size; Cohen's d			0.626		-0.107
<b>Key Secondary Endpoint:</b> SDS Score: LSM (SE) [Disability Scale]		-2.061 (0.2040)	-3.254 (0.3487)	-0.422 (0.3025)	-0.901 (0.2866)
<i>p-value</i>	<i>p=0.004</i>		<i>p=0.0036</i>		NS
Effect size; Cohen's d			0.498		0.311

Note: For Stage 1, baseline is study week 0 and week 5 is study week 5. For Stage 2, baseline is study week 5 and week 5 is study week 10.

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## FDA Comment Regarding Stage 1 of SPCD Trials:

*“We would like to reiterate that we haven’t endorsed any analytical method for SPCD in a confirmatory trial setting. We are continuing making efforts in further understanding its pros and cons from a regulatory perspective. You are encouraged to collect efficacy data from both stages. However, we may determine the efficacy based on data from only Stage 1 if analysis associated with this novel design is still unsettled by the time of your NDA filing.”*

**Source:** Slide from FDA presentation during Alkermes Advisory Committee Meeting held on 11/1/2018.

# Summary of Additional Secondary Endpoints

Additional Secondary Endpoints <sup>1</sup>	Overall	Stage 1 (5 weeks)		Stage 2 (5 weeks)	
		Pbo (n=152)	PIM (n=51)	Pbo to Pbo (n=29)	Pbo to PIM (n=29)
Response Rate <sup>2</sup> , % (n)		25.0% (38)	52.9% (27)	6.9% (2)	6.9% (2)
p-value	<i>p=0.0065</i>		<i>p=0.0002</i>		NS
Remission Rate <sup>2</sup> , % (n)		11.2% (17)	23.5% (12)	3.4% (1)	3.4% (1)
p-value	NS		<i>p=0.0292</i>		NS
CGI-S Score [Clinical Global Severity]	<i>p=0.0084</i>		<i>p=0.0001</i>		NS
CGI-I Score [Clinical Global Improvement]	<i>p=0.0289</i>		<i>p=0.001</i>		NS
SF-12 MCS Score [Mental health]	<i>p&lt;0.0001</i>		<i>p&lt;0.0001</i>		NS
SF-12 PCS Score [Physical health]	NS		NS		NS
DAI-10 Score [Drug attitude]	NS		NS		NS
KSS Score [Daytime sleepiness]	<i>p=0.0205</i>		<i>p=0.0003</i>		NS
MGH-SFI [Sexual functioning]	<i>p=0.0003</i>		<i>p=0.0002</i>		NS
BIS-11 Score [Impulsiveness]	<i>p=0.0075</i>		NS		<i>p=0.0071</i>
SIS Score [Irritability]	NS		<i>p=0.0013</i>		NS

<sup>1</sup>Additional secondary endpoints display nominal p-values.

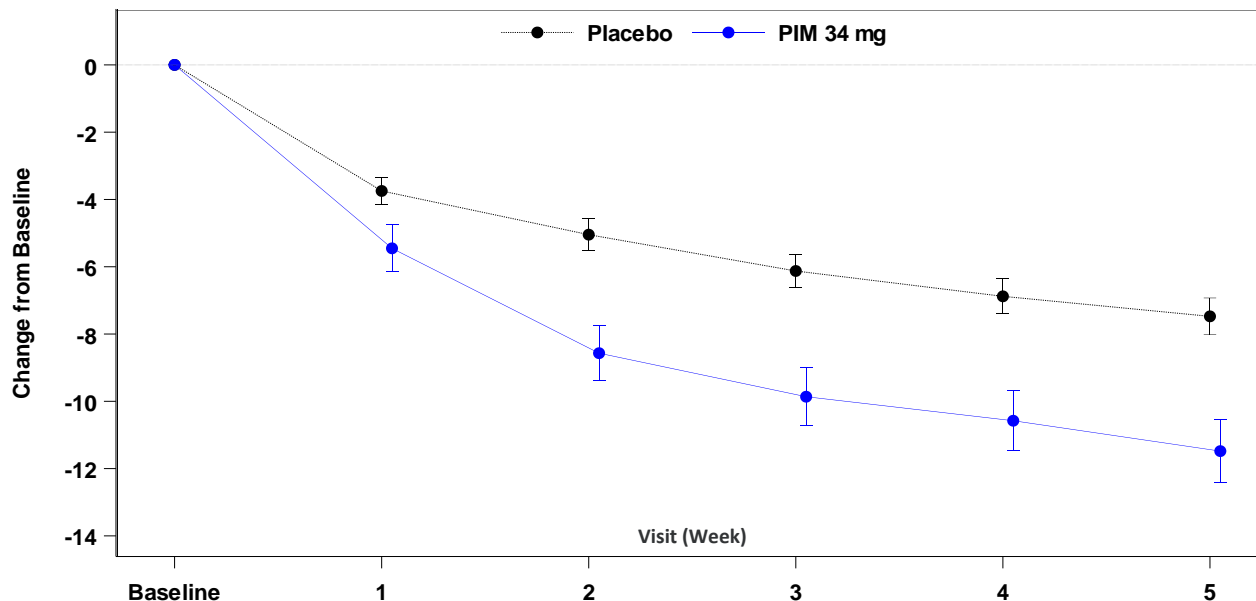
<sup>2</sup>Response rate defined as a 50% or greater reduction on the HAM-D-17 total score; Remission rate defined as HAM-D-17 total score less than or equal to 7.

Note: For Stage 1, baseline is study week 0 and week 5 is study week 5. For Stage 2, baseline is study week 5 and week 5 is study week 10

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# Primary Endpoint: HAMD-17 Stage 1 Results

## HAMD-17 Total Score (Stage 1)



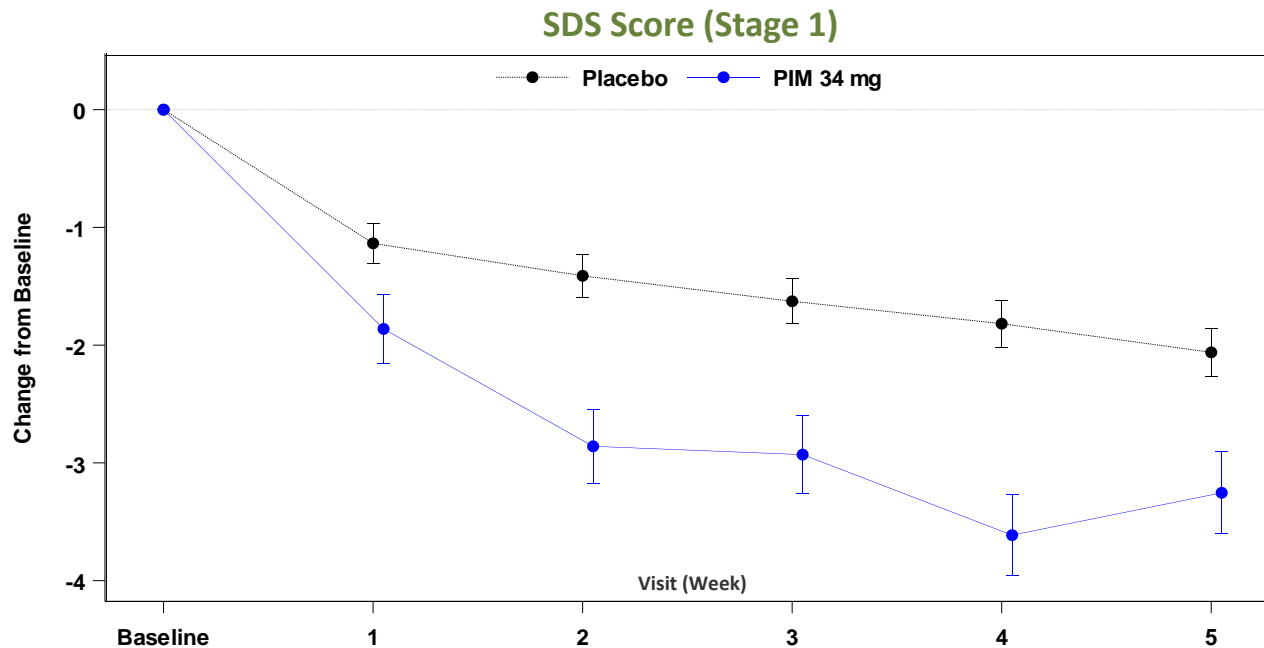
**HAMD-17 at Week 5**  
*p-value = 0.0003*  
*Effect Size = 0.626*

	Baseline	1	2	3	4	5
<b>No. of subjects</b>						
Placebo	152	148	141	135	131	127
PIM	51	49	48	45	44	45
<b>p-value</b>		<b>0.0365</b>	<b>0.0003</b>	<b>0.0002</b>	<b>0.0004</b>	<b>0.0003</b>
<b>Effect Size</b>						<b>0.626</b>

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

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# Key Secondary Endpoint: SDS Stage 1 Results



**SDS at Week 5**  
*p-value = 0.0036*  
*Effect Size = 0.498*

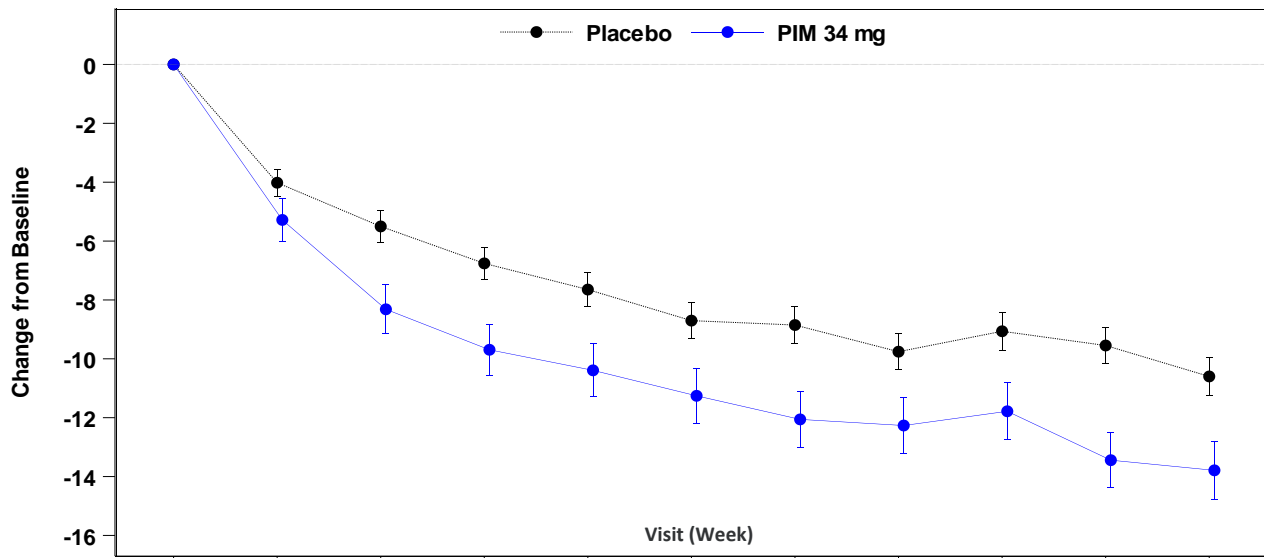
No. of subjects	
Placebo	152      148      141      135      131      127
PIM	51      49      48      45      44      45
<i>p-value</i>	<b>0.0325</b> <b>&lt;0.0001</b> <b>0.0009</b> <b>&lt;0.0001</b> <b>0.0036</b>
<b>Effect Size</b>	<b>0.498</b>

Note: Weekly p-values (except week 5) are nominal  
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# Primary Endpoint for Patients Receiving Continuous Treatment with Pimavanserin or Placebo for 10 Weeks\*



## HAMD-17 Total Score: 10 Weeks (Double-Blind Period)



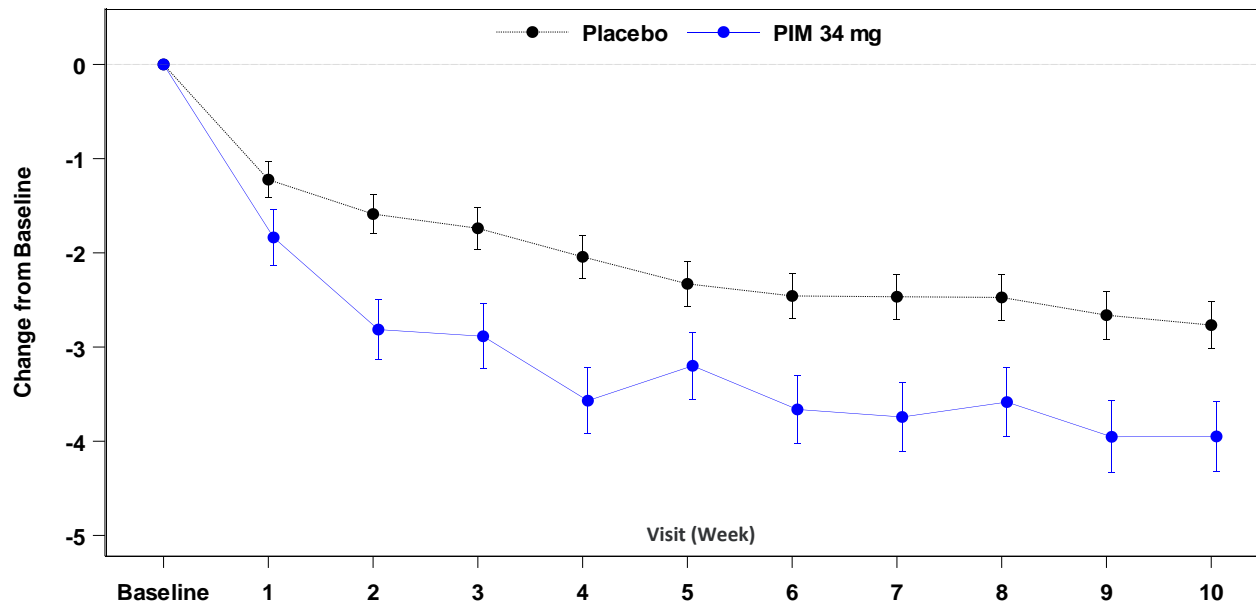
**HAMD-17 at Week 10**  
*p-value = 0.0076*  
*Effect Size = 0.497*

	Baseline	1	2	3	4	5	6	7	8	9	10
<b>No. of subjects</b>											
Placebo	123	119	112	106	102	98	95	88	86	84	85
PIM	51	49	48	45	44	45	43	41	42	40	40
<i>p-value</i>			0.0053	0.0049	0.0122	0.0232	0.0057	0.0285	0.0223	0.0008	0.0076
<b>Effect Size</b>											0.497

\*This was a pre-specified evaluation with the inferential statistics computed post-hoc; all p-values are nominal  
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# Key Secondary Endpoint for Patients Receiving Continuous Treatment with Pimavanserin or Placebo for 10 Weeks\*

## SDS Score: 10 Weeks (Double-Blind Period)



**SDS at Week 10**  
*p-value = 0.0094*  
*Effect Size = 0.469*

	Baseline	1	2	3	4	5	6	7	8	9	10
<b>No. of subjects</b>											
Placebo	123	119	112	106	102	98	96	88	86	84	84
PIM	51	49	48	45	44	45	43	41	42	40	40
<b>p-value</b>			0.0014	0.0061	0.0003	0.044	0.006	0.0039	0.0131	0.0054	0.0094
<b>Effect Size</b>											0.469

\*This was a pre-specified evaluation with the inferential statistics computed post-hoc; all p-values are nominal  
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# Summary of Safety and Adverse Events

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- In the study pimavanserin was well-tolerated
- Discontinuations due to adverse events were 1.2% for pimavanserin and 3.2% for placebo
- One subject in each of the pimavanserin and placebo groups reported serious adverse events, which were deemed not to be related to study drug by the investigators and both of these subjects completed the study
- There were no deaths reported in the study



# Summary of Adverse Events

	Stage 1 (5 weeks)		Stage 2 (5 weeks)	
	Pbo (n=155)	PIM (n=52)	Pbo to Pbo (n=29)	Pbo to PIM (n=29)
<b>Any Patient w/ Adverse Event (AE)</b>	85 (54.8%)	38 (73.1%)	6 (20.7%)	14 (48.3%)
<b>Most Common AEs (&gt;5% in any group)</b>				
Dry mouth	4 (2.6%)	5 (9.6%)		
Nausea	7 (4.5%)	5 (9.6%)		
Sinusitis	--	3 (5.8%)	--	2 (6.9%)
Upper respiratory tract infection	7 (4.5%)	3 (5.8%)	--	2 (6.9%)
Urinary tract infection	1 (0.6%)	3 (5.8%)		
Increased appetite	--	3 (5.8%)		
Headache	14 (9.0%)	5 (9.6%)		
Dizziness	9 (5.8%)	4 (7.7%)		
Sedation	4 (2.6%)	4 (7.7%)		
Arthralgia			--	2 (6.9%)

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# Pimavanserin – Next Steps in MDD

- Plan to meet with the FDA in early 2019
- Given robust positive results, we believe the CLARITY study can serve as one of two pivotal trials required for sNDA submission
- Initiate a Phase 3 Program in 1H 2019
  - Plan to initiate two Phase 3 parallel design, placebo-controlled trials in adjunctive MDD on top of baseline SSRI/SNRI therapy

# Dementia-Related Psychosis (DRP)

Includes Psychosis Associated with Alzheimer's, Parkinson's, Lewy Body, Vascular and Fronto-temporal Dementia



## HIGH UNMET NEED

### No FDA approved treatment

~1.2M people in U.S. have dementia-related psychosis

#### 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** by about one year and carry significant side effects

## CLINICAL PROGRAM

### FDA granted Breakthrough Designation

Demonstrated antipsychotic efficacy in Alzheimer's (Study -019) and Parkinson's (Study -020) patients

Observed **no cognitive impairing effect** after 12-week treatment in Alzheimer's disease psychosis Study -019

#### Phase 3 HARMONY study

- Relapse Prevention Study
- Potential interim results in 2H19



# Schizophrenia – Inadequate Response

Phase 3 ENHANCE Study Ongoing – Adjunctive Therapy



## HIGH UNMET NEED

### One percent of adults

in the U.S. suffer from schizophrenia, a debilitating and lifelong condition

Current Treatment Response

~1/3  
RESPOND

~1/3  
PARTIALLY  
RESPOND

~1/3  
DO NOT  
RESPOND

### Higher probability of polypharmacy may lead to:

- Increased dose-related side effects
- Poor compliance
- Subsequent relapse

## CLINICAL PROGRAM

### Pimavanserin added to background

**antipsychotic** Exploring potential to augment efficacy, improve treatment response, and lessen the side effects associated with current polypharmacy

Positive Phase 2 data in co-therapy study in schizophrenia

### Phase 3 ENHANCE study

- Six-week, randomized, double-blind, placebo-controlled adjunctive therapy study
- Enrolling ~380 schizophrenia patients with inadequate response to current antipsychotic treatment
- Expect to complete enrollment 1H19
- Data expected mid-2019

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# Schizophrenia – Negative Symptoms

Phase 2 ADVANCE Study Ongoing – Adjunctive Therapy



## HIGH UNMET NEED

### No FDA-approved treatment

~40% to 50% of schizophrenia patients suffer prominent negative symptoms:

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

Current antipsychotics target positive symptoms with minimal effect on negative symptoms

Significant side-effect burden and poor compliance:

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

## CLINICAL PROGRAM

### Pimavanserin added to background antipsychotic

Exploring potential to treat negative symptoms in schizophrenia

Prior Phase 2 study: Positive effect on PANSS negative symptom subscale when dosed as adjunct to risperidone

Other 5-HT<sub>2A</sub> related blockers have shown effect on negative symptoms

### Phase 2 ADVANCE study

- 26-week randomized, double-blind, placebo-controlled adjunctive therapy study
- Enrolling ~380 schizophrenia patients with predominant negative symptoms
- Expect to complete enrollment 2H19



# Trofinetide – Rett Syndrome

Exclusive North American license agreement with Neuren Pharmaceuticals



## HIGH UNMET NEED

**Debilitating neurologic rare disease**  
**No FDA-approved treatment**

**Rett syndrome 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

**Rett is caused by mutations on the X chromosome on a gene called MeCP2**

Rett syndrome occurs worldwide in approximately one in every 10,000 to 15,000 female births

## CLINICAL PROGRAM

**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

**Prior Phase 2 study:** Statistically significant improvement on RSBQ\* and CGI-I\* in girls aged 5 – 15 years of age with Rett syndrome

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

**Plan to initiate Phase 3 double-blind, placebo-controlled study in 2H19**

- Enrolling ~180 girls with Rett syndrome
- Co-primary endpoints: RSBQ and CGI-I
- Potential to submit NDA (2021) with positive results

\*RSBQ = Rett Syndrome Behaviour Questionnaire; CGI-I = Clinical Global Impressions Scale-Improvement  
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# Commercial Update

Michael Yang  
Chief Commercial Officer



**FDA Approval and Launch**  
of new NUPLAZID dosing  
formulation (34 mg capsule)  
and strength (10 mg tablet) to  
advance treatment options



**FDA Issues Statement**  
Reaffirming the positive  
benefit-risk profile of  
NUPLAZID



**ACADIA Launches**  
**NUPLAZID Straight Talk**  
website to better inform  
patients and caregivers on the  
facts of NUPLAZID as the first  
and only approved medicine to  
treat hallucinations and  
delusions associated with  
PD Psychosis

ONCE-DAILY  
**NUPLAZID**<sup>®</sup>  
(pimavanserin) 34mg capsules  
**straightTALK**

**Branded DTC Campaign**  
to build awareness of  
potential benefits of  
NUPLAZID for patients



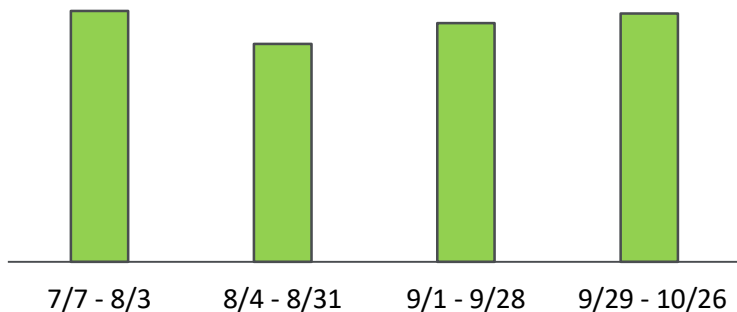
## Activities to Revitalize Growth Trajectory in New Patient Starts with NUPLAZID

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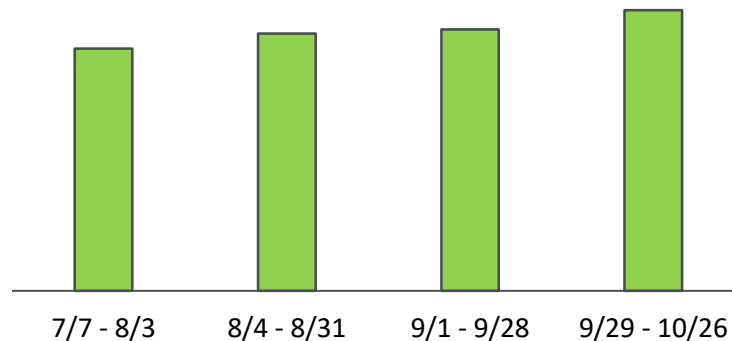


# Growth Trends by Channel

**Specialty Pharmacy New Patient Starts  
(Weekly Avg)**



**Long-Term Care Specialty Distributor Bottles  
(Weekly Avg)**



- Weekly average of new patient starts are now trending higher in the specialty pharmacy channel
- Continued growth in long-term care channel

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## Finance Update

Elena Ridloff  
Interim Chief Financial Officer

# 3Q18 Financial Highlights



\$ Millions, Except EPS

	3Q18 (GAAP)	3Q17 (GAAP)	YoY Change
<b>Total Revenue</b>	\$58.3	\$35.6	+64%
<b>Cost of Product Sales, License Fees and Royalties</b>	\$5.4	\$3.2	+67%
<b>R&amp;D</b>	\$53.1	\$36.4	+46%
<b>SG&amp;A</b>	\$61.1	\$61.6	-0.1%
<b>Net Loss</b>	(\$62.1)	(\$65.2)	+5%
<b>Basic and FD Shares Outstanding (M)</b>	125.0	122.5	+2%
<b>EPS</b>	(0.50)	(0.53)	+6%

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# FY 2018 Financial Guidance



<b>FY 2018</b>	<b>Updated Guidance</b>	<b>Prior Guidance</b>
<b>NUPLAZID NET SALES</b>	\$220 to \$225M	\$210 to \$225M
<b>YE 2018 CASH*</b>	\$160 to \$170M	\$155 to \$170M

\*Cash, cash equivalents and investment securities

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# CEO Closing Remarks

Steve Davis  
President and CEO

# Committed to Executing on Our Key Priorities



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

- ✓ Delivered positive results for pimavanserin as an adjunct therapy in major depressive disorder
- ✓ FDA issued a clear statement reaffirming the positive benefit-risk profile of NUPLAZID
- ✓ Successful launch of NUPLAZID once-daily 34 mg capsule
- ✓ Advanced late-stage clinical pipeline programs in areas that have significant unmet needs in CNS

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## Q&A

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