

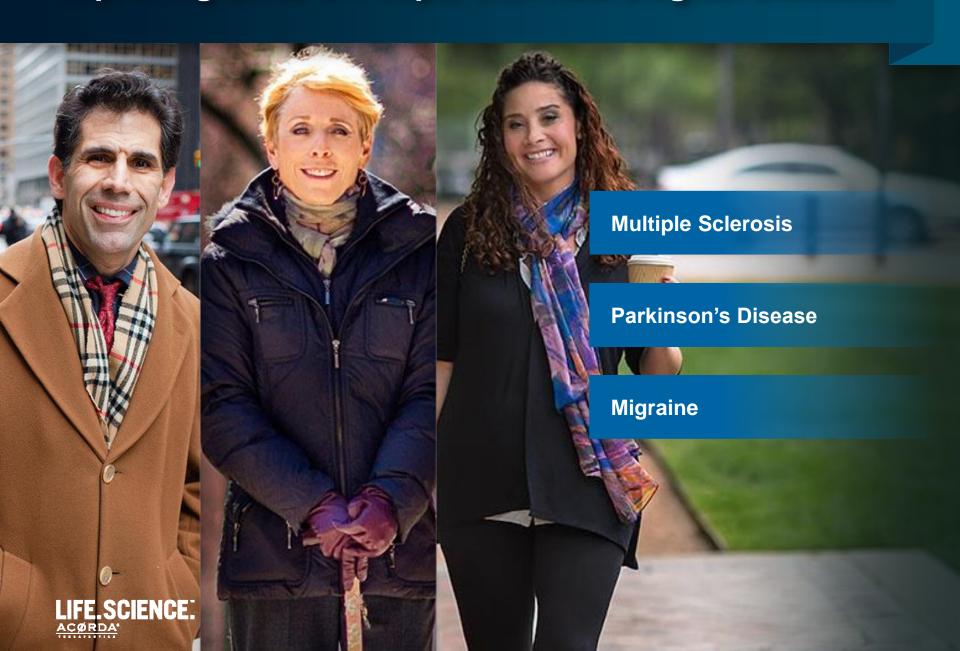
### **Forward Looking Statement**

This presentation includes forward-looking statements. All statements, other than statements of historical facts, regarding management's expectations, beliefs, goals, plans or prospects should be considered forward-looking. These statements are subject to risks and uncertainties that could cause actual results to differ materially, including: the ability to realize the benefits anticipated from the Biotie and Civitas transactions, among other reasons because acquired development programs are generally subject to all the risks inherent in the drug development process and our knowledge of the risks specifically relevant to acquired programs generally improves over time; the ability to successfully integrate Biotie's operations and Civitas' operations, respectively, into our operations; we may need to raise additional funds to finance our expanded operations and may not be able to do so on acceptable terms; our ability to successfully market and sell Ampyra (dalfampridine) Extended Release Tablets, 10 mg in the U.S.; third party payers (including governmental agencies) may not reimburse for the use of Ampyra or our other products at acceptable rates or at all and may impose restrictive prior authorization requirements that limit or block prescriptions; the risk of unfavorable results from future studies of Ampyra or from our other research and development programs, including CVT-301 or any other acquired or in-licensed programs; we may not be able to complete development of, obtain regulatory approval for, or successfully market CVT-301, any other products under development, or the products we acquired with the Biotie transaction; the occurrence of adverse safety events with our products; delays in obtaining or failure to obtain and maintain regulatory approval of or to successfully market Fampyra outside of the U.S. and our dependence on our collaborator Biogen in connection therewith; competition; failure to protect our intellectual property, to defend against the intellectual property claims of others or to obtain third party intellectual property licenses needed for the commercialization of our products; and failure to comply with regulatory requirements could result in adverse action by regulatory agencies.

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### **Improving Lives of People with Neurological Diseases**



### **Clinical Pipeline**

THERAPY	INDICATION	PHASE 1	PHASE 2	PHASE 3	
CVT-301	Parkinson's Disease				
TOZADENANT	Parkinson's Disease				
SYN120	Parkinson's Disease				
BTT1023 (timolumab)	Primary Sclerosing Cholangitis (PSC)				
CVT-427	Migraine				
rHlgM22	MS				



### 2016 Achievements



#### **CVT-301 Development Program**

- Last patient out of Phase 3 efficacy study
- Phase 3 efficacy and long term safety data expected in 1Q17;
   NDA expected in 2Q17



#### **CVT-427 for Migraine**

- Presented positive Phase 1 data at American Headache Society
- Phase 2 study initiation expected in 2H 2017



#### **Acquisition of Biotie Therapies**

- Tozadenant in Phase 3 for Parkinson's disease
- SYN120 in Phase 2
- BTT1023 in PSC
- Royalty stream from Selincro (Lundbeck)

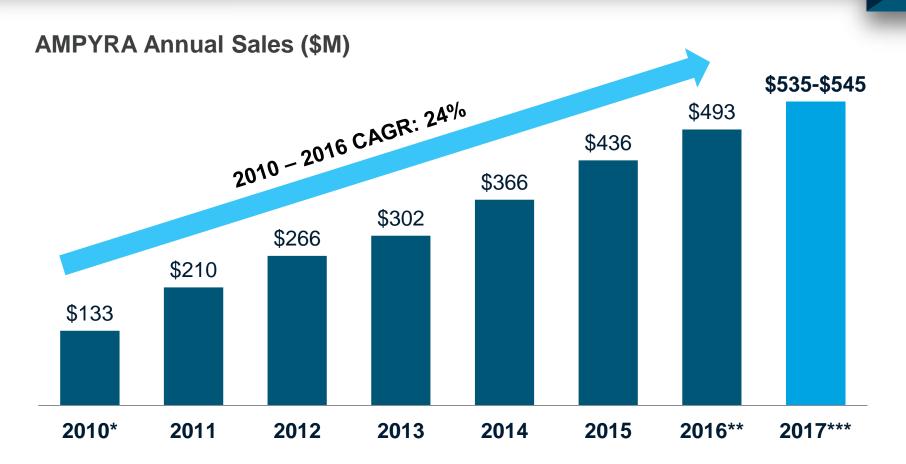


#### **AMPYRA 2016 Growth**\*

- Net sales of \$493 Million
- Net sales growth of 13%



### AMPYRA (dalfampridine) for Multiple Sclerosis





\*Ten months, Mar – Dec 2010 \*\*Unaudited; subject to audited financials \*\*\* 2017 guidance provided on January 9, 2017



### **CVT-301** in Parkinson's Disease

LIFE.SCIENCE.

#### **CVT-301 Overview**





#### **Inhaled Levodopa**

- Self-administered, inhaled medication
- Utilizes ARCUS® technology to deliver specific doses of dry powder L-dopa



#### **Positive Phase 2b Efficacy Data**

- Results show potential to treat OFF periods
- Separation vs. placebo observed at 10 minutes after dosing and was durable for at least an hour
- Clinically important reductions in UPDRS Part III at both tested doses

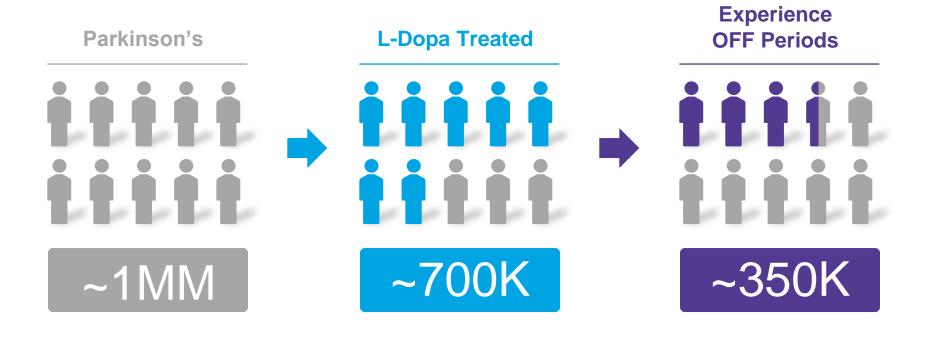


#### **Phase 2b Safety Profile**

- No treatment-associated AEs on lung function
- No serious AEs overall
- No increase in dyskinesia during at-home use



### **OFF Periods: Unmet Medical Need**





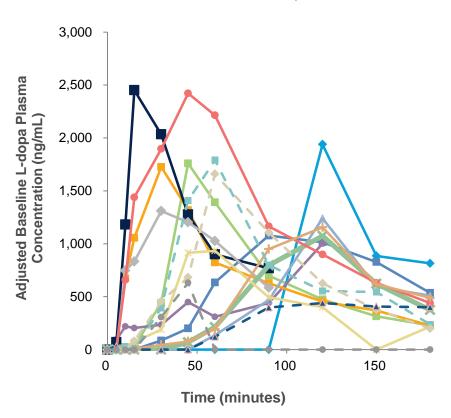
Source: National Parkinson's Foundation

= 100,000 people

### L-Dopa Pharmacokinetics

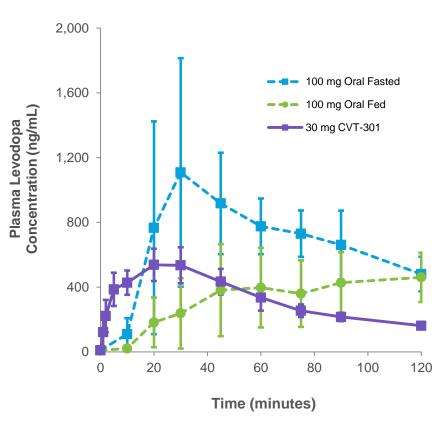
#### **Current Oral Standard of Care**

Data from Phase 2a in fasted PD patients



#### **CVT-301 Profile**

Data from Phase 1 trial in healthy volunteers



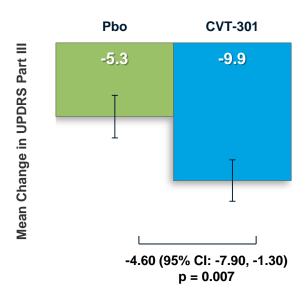


Source: Lipp et al., Sci. Transl. Med. October 2016

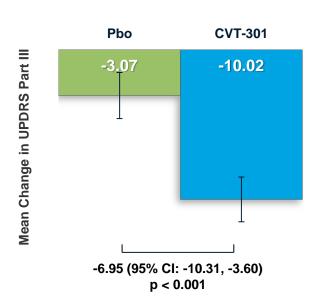
# Phase 2b Study Achieved Primary Endpoint UPDRS Part III

#### Clinically important reductions at both tested doses

Visit 4: CVT-301 35mg or Pbo



Visit 6: CVT-301 50mg or Pbo



## UPDRS Part III Clinically Important Differences (CID)\*:

2.5pts = Minimal CID

5.2pts = Moderate CID

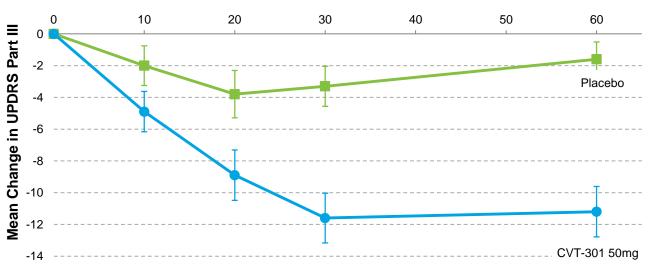
10.8pts = Large CID



# Phase 2b Data Showed Separation vs. Placebo Observed at 10 Minutes

#### **Visit 6 – CVT-301 50mg dose**

Time (minutes)



UPDRS Part III
<b>Clinically Important</b>
Differences (CID)*:

2.5pts = Minimal CID

5.2pts = Moderate CID

10.8pts = Large CID

	10 min	20 min	30 min	60 min
Diff vs Pbo Mean (SEM)	-3.56 (1.62)	-5.68 (2.04)	-8.43 (1.90)	-9.59 (1.83)
p-value	0.0309	0.0068	<0.0001	<0.0001

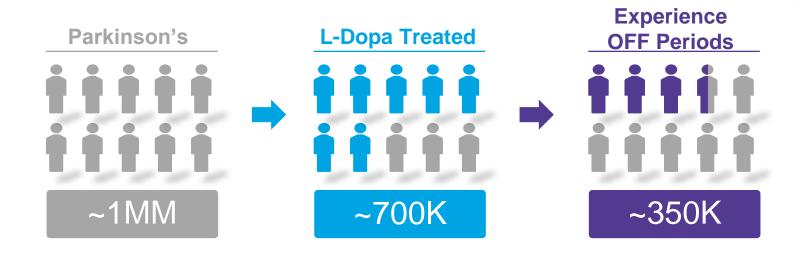


### **CVT-301 Phase 2b Safety Profile**

Treatment-Emergent Adverse Event, n (%)	Placebo Group (n=43)	CVT-301 Group (n=43)
Dizziness	2 (5)	3 (7)
Cough	1 (2)	3 (7)
Nausea	0	3 (7)
Headache	2 (5)	2 (5)
Peripheral edema	1 (2)	2 (5)
Anxiety	0	2 (5)
Discolored sputum	0	2 (5)



### **CVT-301 U.S. Market Opportunity**



Projected U.S. Peak Sales in Excess of \$500 million







### **Tozadenant for Parkinson's Disease**



### **Tozadenant Overview**

### Mechanism of Action

- Adenosine 2A (A2A) receptor antagonist
- Expressed in high concentration in basal ganglia and play an important role in regulating motor function

#### Robust Phase 2b Data

- Statistically significant and clinically meaningful OFF time reduction in people treated with multiple PD therapies
- Improvement in multiple secondary endpoints

### Phase 3 Enrolling

- Phase 3 study design similar to Phase 2b
- Special Protocol Assessment (SPA)
- Topline data expected 1Q 2018



### **Positive Phase 2b Trial**

Tozadenant (SYN115) in patients with Parkinson's disease who have motor fluctuations on levodopa: a phase 2b, double-blind, randomised trial



Robert A. Flasser, C. Warren Grovers, Karl D. Kelturtz, Erremans die Passcher, Any Disco-Andersal, Mark Leis, Okssandr Karyelkin, Ann Nacing Chris Roberty OverMays, Christopher Kenney Stephen Sondali

### THE LANCET Neurology

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nero, phase 2b, randomised, double-blind, placebo-controlled, parallel-group. http://m.mi.orgoutne. i in levedopa-meand patients with Parkinson's disease who had motor mans 60, 120, 180, or 240 mg or marching placebo twice daily for 12 weeks. Network of non-trivial and realizations. and patients were marked to creament assignment. The primary operation Mourage Standard Cons. surs per day spens in the off-state (assessed from Parkinson's disease diaries surred as Clinical Irials gov, number NCT01283594.

(mean age 63-3 [SD 8-3] years; mean duration of Parkinson's disease. Next the back we have the other day data and 337 completed study treatment. Compared with placebo. shicad in the combined vocaderum 120 mg swice-daily and 180 mg twice (S=0.0000), the recaderum 120 mg twice-daily group (-1.1 h, -1.5 h -0.4), which daily group (-1.2 h, -1.5 h -0.4) fixed with (S=0.000). The most common (S=0.000) fixed most common (S=0.000) fixed (S=0.0Saltnessta (seven [896] of 84 partients in the placebo group, 13 [1696] of 82 in the Minarmen, Seato of

126 mg soles-daily group, and 17 (20%) of 85 in the 180 mg soles-daily group), named (three [4%], 9 (11%), and meters is although son [1296], and dizenness (one [196], four [96], and 11 [196]). To admin 60 mg twice daily was not associated with \$600m, 0; Geneta (\$60, September 1965), September 1965, Sep a significant reduction in oil-time, and to-admant 240 mg twice daily was associated with an increased rate of discontinuation because of adverse events (17 [2090] of 84 patients).

interpretation Totalemant at 120 or 180 mg swice daily was generally well tolerated and was effective at reducing off-time. Further investigation of social ename creatment in phase 3 trials is warranted.

Funding Blode Therapies.

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of Central Neurology, Increase eroublesome dyskinesta. However, preiadenane Levelopa remains the gold standard for symptomatic was not effective in phase 3 clinical trials, and moneta, Levelopa remains encements of Parkinson's disease. However, long-term iterade-plane produced mixed results.<sup>54</sup> Although terms of the control o stratment is associated with the development of mount intradefilline was not approved by the US Food and Drug Bank Temper, took too Pacenarium and dyskinosias. In advanced disease, drugs Administration in 2008, it was approved as an adjunct to A base 20 (Decoration of A base 20

assessed in a phase 2a smdy that used a 2x2 crossover temperatures Admostne A. recipiors are highly localised so design in which patients with mild Parkinson's disease 2-blank/lane timensy embendralitismytic sintaisiyalibdal yamittooluayitic acid worte randomly assigned ofther to I week of socialisman, load-listia helman (GARA) containing neurons that form part of the indirect. I work of washout, and I work of placebo, or so the Green National Patricus. basal gaught pathway. Sumulatory A., and inhibitory D. reverse order. The results showed that cappting speed was interest testing doparning receptors are colocalised on these neurons and factor on to-admine 60 mg sevice daily than on placebo factor in the color modulast indirect pathway activity. Results of phase 2 both before (5%, p-0-03) and during a levelope frameginent-at-at-

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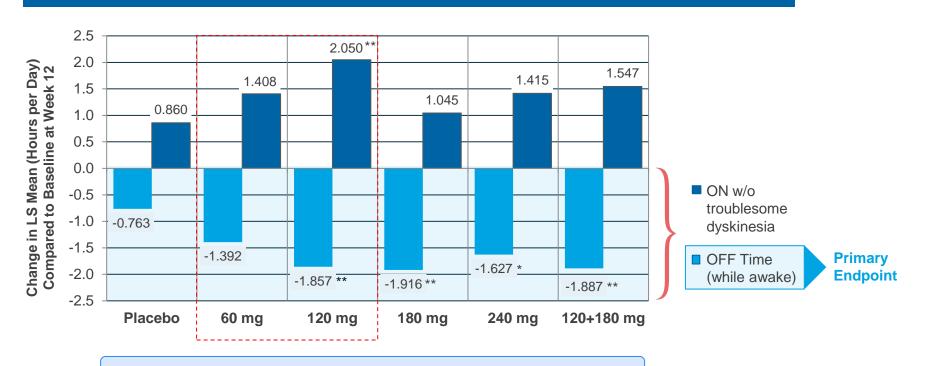
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### **Phase 2b Met Primary Endpoint**

#### **Patient Diary Data: Less OFF Time and More ON Time**



120mg dose in Phase 3 provides best balance between OFF time and quality ON time

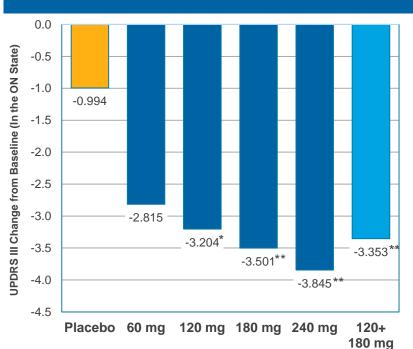


Indicates raw p-value <0.05 relative to placebo

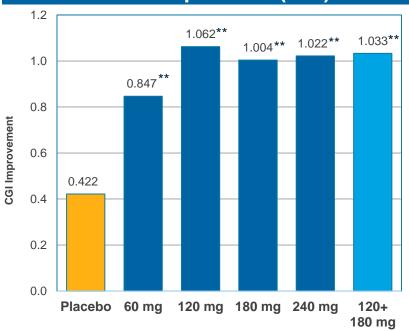
<sup>\*\*</sup> Indicates raw p-value <0.01 relative to placebo

### Phase 2b Key Secondary Endpoints

#### Significant Improvement in UPDRS III



### Significant Improvement in Clinician Global Impression (CGI)



Change from baseline to end of treatment (week 12, mITT population)



Indicates raw p-value <0.05 relative to placebo

Indicates raw p-value <0.01 relative to placebo

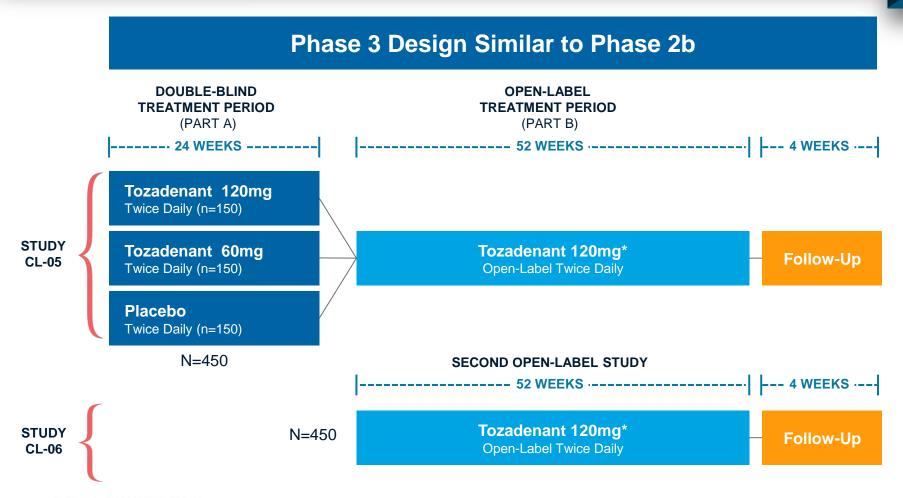
### **Phase 2b Safety Data**

	Placebo (n=84)	60 mg (n=85)	120 mg (n=82)	180 mg (n=85)	240 mg (n=84)
Patients with at least 1 serious AE	3	1	3	2	4
Deaths	0	1	0	2	3
Patient discontinuations due to TEAE	3	7	10	10	17
TEAE reported by at least 5% of patients					
Dyskinesia	7	12	13	17	17
Nausea	3	5	9	10	5
Dizziness	1	4	4	11	8
Constipation	0	8	9	3	5
Worsening Parkinson's disease	9	4	6	8	4
Insomnia	2	2	7	7	5
Fall	4	4	3	7	3
Flushing	2	2	3	6	5
Headache	1	4	4	5	3
Blood creatine phosphokinase increased	2	4	2	5	3
UTI	4	4	5	4	1
Sudden onset of sleep	5	3	2	3	4
Back pain	4	5	1	3	2



### **Ongoing Phase 3 Program**

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### **Early Stage Clinical Pipeline**



#### CVT-427 (migraine)

- Phase 1 data showed median TMAX of ~12 minutes for all doses compared to 1.5 hours for oral tablet and 3 hours for nasal spray
- No serious AEs reported after administration; most commonly reported TEAEs were cough, chest discomfort, headache and feeling hot
- Phase 2 study planned for 2H 2017



#### SYN120 (Parkinson's disease dementia)

- Potent and selective antagonist of 5HT6 and 5HT2a receptor;
   potential activity for symptoms of dementia and psychosis
- Phase 2 study currently enrolling in partnership with MJFF; last patient out expected 2H 2017



### **Early Stage Clinical Pipeline**



#### BTT1023 (primary sclerosing cholangitis)

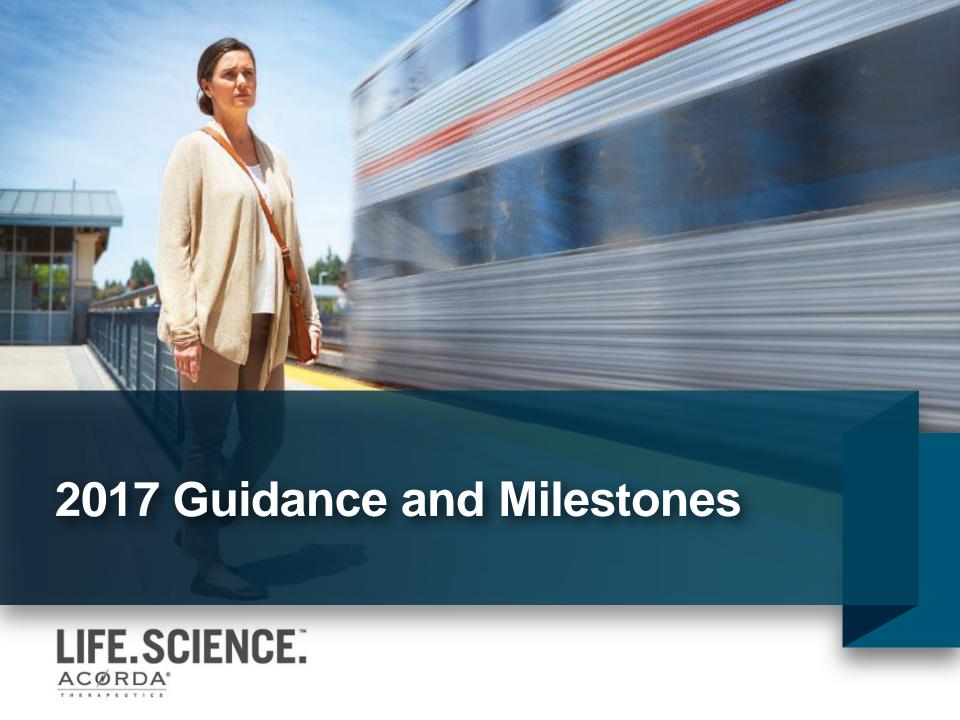
- Fully human monoclonal antibody that binds to vascular adhesion protein-1 (VAP-1)
- PSC is a chronic and progressive fibrotic disease of the liver
- Phase 2 Proof-of-Concept study currently enrolling patients



#### rHIgM22 (multiple sclerosis)

- Remyelinating monoclonal antibody for treatment of MS
- Phase 1, single ascending dose study in acute MS relapses currently enrolling
- Study completion expected 2H 2017





### 2017 Guidance



AMPYRA Net Sales \$535 - \$545 million



R&D Expense \$185 - \$195 million



\$195 - \$205 million



## Key Events\*

Phase 3 Efficacy and 12-Month Safety Data for CVT-301	1Q 2017
AMPYRA IP Decisions (District Court and IPR)	1Q 2017
NDA Filing for CVT-301	2Q 2017
Initiate Open-Label Safety Study for Tozadenant	1H 2017
Initiate Phase 2 Study for CVT-427 in Migraine	2H 2017
Marketing Authorization Application (MAA) Submitted for CVT-301	4Q 2017
Phase 3 Efficacy Data for Tozadenant	1Q 2018
Phase 2 Proof of Concept Data for SYN120	1Q 2018



<sup>\*</sup> Expected timelines

### **2017 Priorities**

Advance Late Stage Parkinson's Programs Maximize AMPYRA Value

**Business Development** 



