

# Strongbridge Biopharma plc

September 2019





# Forward-looking statements

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These forward-looking statements involve known and unknown risks, uncertainties, and other factors that may cause the Company's actual results, performance, or achievements or industry results to be materially different from those contemplated, projected, forecasted, estimated or budgeted, whether expressed or implied, by these forward-looking statements. Given these risks and uncertainties, investors should not place undue reliance on forward-looking statements as a prediction of actual results. A discussion of certain of these risks may be found in the filings the Company makes with the U.S. Securities and Exchange Commission. None of these forward-looking statements constitutes a guarantee of the future occurrence of such events or of actual results. These statements are based on data, assumptions, and estimates that the Company believes are reasonable.

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# Strongbridge portfolio

		Indication/ Target Disease	Pre-clinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Rights
Rare Endocrinology	<b>RECORLEV™</b> (levoketoconazole)	Endogenous Cushing's syndrome	Phase 3					 Global
	<b>veldoreotide modified-release</b>	Conditions modifiable through activation of somatostatin receptors, such as Cushing's disease and neuroendocrine tumors	Pre-clinical	Immediate Release Formulation Completed Phase 2				 Global
Rare Neuro-muscular	<b>KEVEYIS®</b> (dichlorphenamide)	Primary Periodic Paralysis	Marketed					 US
Asset Sold	<b>MACRILEN™</b> (macimorilen)	Adult Growth Hormone Deficiency diagnosis	Marketed					 US & Canada

# Investment highlights

- **Revenue generating rare disease company**
  - Focused on building a portfolio of vertical, therapeutically-aligned franchises
- **Established commercial infrastructure in two rare disease therapeutic areas**
  - 23 person neuromuscular field team dedicated to Keveyis
  - 23 person rare endocrine field team for Macrilen; funded by Novo Nordisk\*
- **Late-stage clinical asset Recorlev**
  - Reported positive pivotal SONICS Phase 3 trial results
  - Anticipate LOGICS Phase 3 trial top-line results at end of Q1 2020
  - NDA submission planned for end of Q3 2020
- **Strong business development capabilities**
  - Proven ability to identify, evaluate and transact efficiently and effectively
- **Seasoned management team**
  - Extensive experience in rare disease drug development and product launches

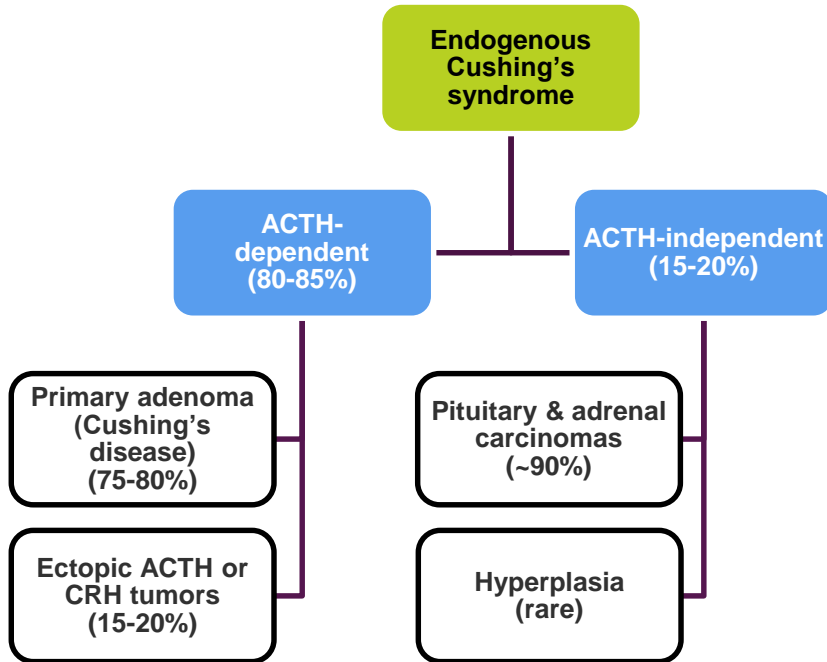
\*Receiving ~\$7-8 million per year from Novo Nordisk; funding for three years beginning December 2018

# Recorlev

(levoketoconazole)

# Endogenous Cushing syndrome overview

Underlying cause is chronic exposure to excess serum cortisol due to any of several etiologies



## Cushing syndrome affects the whole body



Psychosis, impaired memory, sleep disturbance, depression, anxiety



Heart attacks, stroke, high blood pressure, high cholesterol, vein clots



Overweight/obesity, facial, neck and abdominal fat accumulation, diabetes



Muscle and skin atrophy



Osteoporosis



# Cushing's syndrome unmet need and prevalence

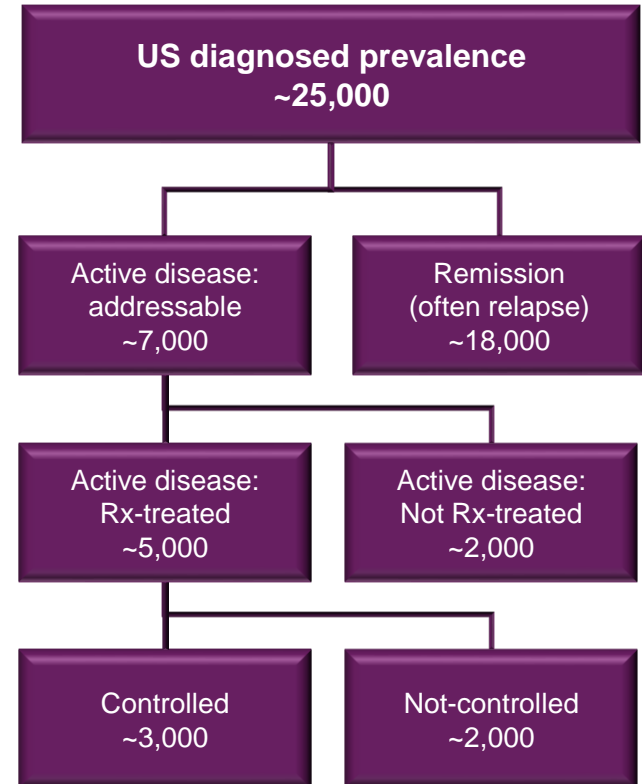
## Unmet need and burden of illness

Per a 2017 study\* of 224 patients, cortisol control was not achieved with any treatment modality—including surgery, radiation and medicines—in more than half of the subjects:

- » 49.1% control achieved
- » 29.9% control not achieved
- » 21.0% indeterminate

Cushing's disease patients have:<sup>1\*</sup>

- » 2-5x higher incidence rates of comorbidities (eg, cardiovascular, endocrine, musculoskeletal, and mental health conditions)
- » 7x higher medical costs
- » 4x higher pharmacy costs



# Recorlev (levoketoconazole) overview

- Pure 2S,4R enantiomer of ketoconazole, a steroidogenesis inhibitor used “off-label” to treat endogenous Cushing’s syndrome
  - Ketoconazole is not approved for Cushing’s syndrome in the US
- Administered orally
- Demonstrated favorable efficacy, safety, and tolerability in pivotal Phase 3 SONICS trial
- Received orphan drug designation in the US and EU
  - Pursuing 505(b)2 approval pathway



# Pivotal Phase 3 SONICS trial



**DOSE TITRATION:**  
2 to 21 weeks

**MAINTENANCE:**  
6 months

**EXTENDED EVALUATION:**  
6 months

Titrate in 150 mg increments up to max 600 mg 2x daily until mUFC normalization is achieved

Maintain mUFC normalization with fixed therapeutic dose

94 patients enrolled

77 completed dose titration

61 completed maintenance

46 completed extended evaluation

Primary endpoint and key secondary endpoints measured at end of maintenance phase

# SONICS achieves statistical significance in primary and key secondary endpoints

- Primary endpoint achieved statistical significance with 30% of patients achieving mUFC normalization without dose increase (95% CI: 21%, 40%; p=.0154), ITT analysis
- Six key cardiovascular secondary endpoints achieved statistical significance
  - Improvements in HbA1c and fasting blood glucose were more pronounced among patients with diabetes mellitus

Outcome Measure at End of Maintenance Phase	Baseline Mean, (n)	Mean Change From Baseline <sup>†</sup> , (n)	Adjusted* p-value of reductions from Baseline
Fasting Blood Glucose	5.8 mmol/L, (76)	-0.7, (50)	<0.0001
Hemoglobin A1c	6.0%, (77)	-0.4, (55)	<0.0001
Total cholesterol	5.7 mmol/L, (77)	-1.1, (53)	<0.0001
LDL-cholesterol	3.3 mmol/L, (77)	-1.0, (53)	<0.0001
HDL-cholesterol	1.6 mmol/L, (77)	-0.2, (53)	<0.0001
Body Weight	82.1 kg, (77)	-5.1, (54)	<0.0001

\*Hochberg adjustment applied to p-values to control type 1 error

†Reductions from baseline based on least squares mean changes from repeated measures model

# Expanded mUFC “real world” analysis further supports Recorlev’s efficacy benefit and duration of effect

	End of Maintenance Phase (6 months)	End of Extended Evaluation Phase (12 months)
Responder analysis of maintenance completers with mUFC data and normalization or $\geq 50\%$ mUFC reduction from baseline	76% (42/55) *	68% (30/44) **

\* Data based on 55 maintenance phase completers with both baseline and month 6 mUFC data available.

\*\*An observed-case analysis of completers was used to evaluate mUFC responders in extended evaluation phase. Data based on 44 extended evaluation phase completers with both baseline and month 12 mUFC data available. Key protocol differences in extended evaluation phase compared to maintenance phase included (i) investigators instructed to alter daily dose as needed in extended evaluation to maintain cortisol control and manage side effects and (ii) clinical visits every three months (compared to monthly in maintenance phase)

# No unexpected adverse events after 6 months of treatment

Most commonly reported treatment-emergent adverse events with an incidence  $\geq 15\%$

Adverse Event	% of enrolled (N=94)
Nausea	33%
Headache	29%
Peripheral edema	19%
Hypertension	19%
Fatigue	18%
ALT increased*	17%
Diarrhea	16%
Arthralgia	15%

Adverse Events of Special Interest
Liver-related (7%)
QTc prolongation (7%)
Adrenal insufficiency (3%)

16 (17%) subjects discontinued prior to study completion due to an adverse event

\*Includes all alanine aminotransferase (ALT) increases reported as an adverse event regardless of level or relationship to drug. A subset of these ALT increased events was also reported as adverse events of special interest.

# Favorable liver safety findings after 12 months of maintenance therapy

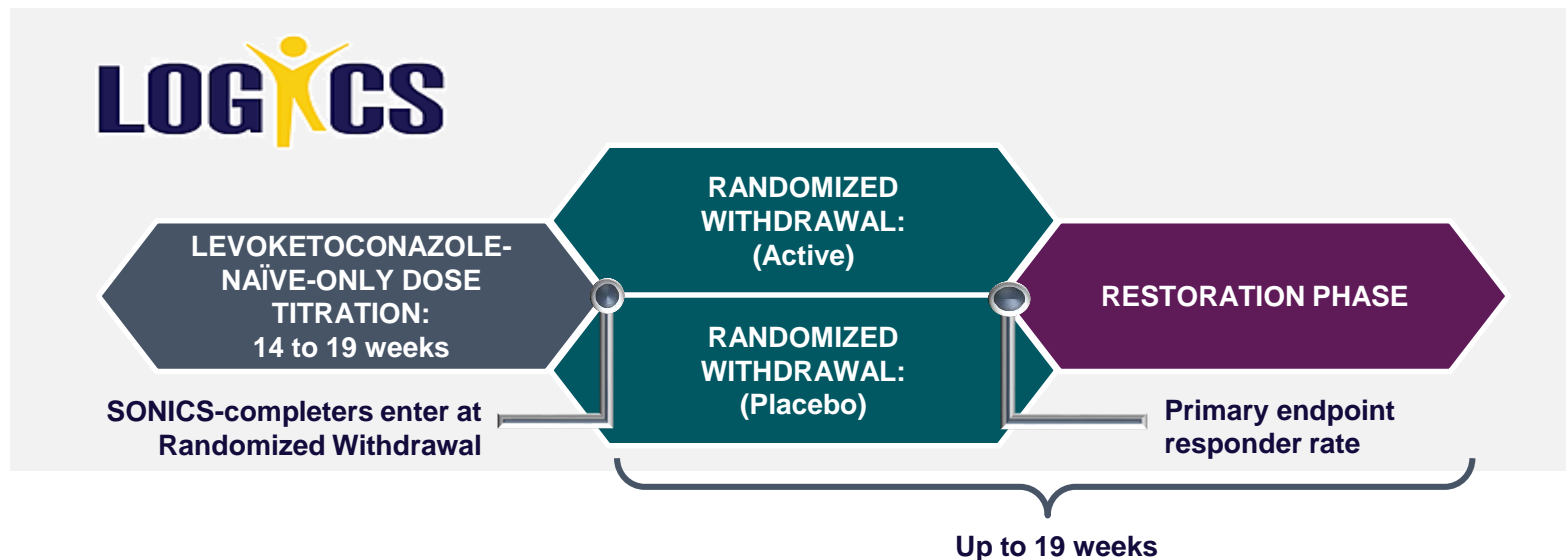
	Recorlev
ALT >3x ULN (includes those > 5x ULN)	10.6%
ALT >5x ULN	3.2%
Total bilirubin values > 1.5x ULN	0%

## SONICS LFT Monitoring Protocol

At least once every two weeks during dose titration. After the therapeutic dose is established, monthly for six months; then every three months thereafter.

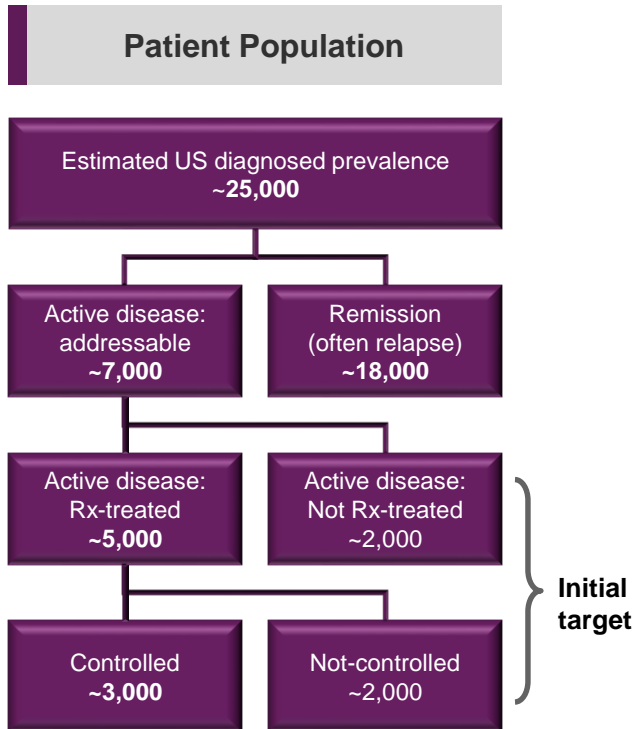
- Only 10.6% of patients had liver enzyme elevation >3x ULN, all of which occurred on or before Day-60 visit of maintenance
- All were reversible upon discontinuation without clinical sequelae
- No transaminases >20 x ULN

# LOGICS Phase 3 placebo controlled trial



- **Enrollment** - up to 54 patients
- **Primary endpoint** - Proportion of patients losing prior-established therapeutic response to levoketoconazole (as measured by mUFC) during randomized withdrawal
- **Top-line results** – anticipated end of Q1 2020

# Recorlev U.S. commercial opportunity



- SONICS data support Recorlev positioning for both drug-naïve patients and patients on other drugs, including approximately 2,000 off-label ketoconazole patients
- Recorlev profile supports pricing in the currently established Cushing's drug pricing corridor of ~\$200K-\$500K annually
- Current FDA-approved drugs for Cushing's are not generally managed by payers – little-to-no requirement for a generic fail-first or step edit, including off-label ketoconazole
- US Cushing syndrome market assessment and Recorlev commercial opportunity assessment underway

Ongoing Macrilen / endocrinology presence may accelerate Recorlev's time to peak penetration

# Ketoconazole off-label use in U.S. in Cushing's syndrome is unsupported by adequate evidence

<b>Indications</b>	Last-line anti-fungal, not indicated for Cushing's syndrome	Ketoconazole Tablets should be used only when other effective antifungal therapy is not available or tolerated...Ketoconazole Tablets are indicated for the treatment of the following systemic fungal infections in patients who have failed or who are intolerant to other therapies...." <sup>1</sup>
<b>Dosage and administration</b>	Limited 6-month course, 400-mg max dose, 200-mg strength, once daily	"The recommended starting dose of Ketoconazole Tablets is a single daily administration of 200 mg (one tablet). If clinical responsiveness is insufficient within the expected time, the dose of Ketoconazole Tablets may be increased to 400 mg (two tablets) once daily.... The usual duration of therapy for systemic infection is 6 months." <sup>1</sup>
<b>Boxed warnings</b>	Hepatotoxicity; QT prolongation and drug interactions leading to QT prolongation	ALT Monitoring: "During the course of treatment, serum ALT should be monitored weekly for the duration of treatment. If ALT values increase to a level above the upper limit of normal or 30 percent above baseline, or if the patient develops symptoms, ketoconazole treatment should be interrupted." <sup>1</sup>
<b>Adverse reactions to unapproved uses</b>	FDA admonition of off-label use	"Ketoconazole has been used in high doses for the treatment of advanced prostate cancer and for Cushing's syndrome when other treatment options have failed. The safety and effectiveness of ketoconazole have not been established in these settings and the use of ketoconazole for these indications is not approved by FDA." <sup>1</sup>

1. Excerpted from Teva Pharmaceuticals USA, Inc. Ketoconazole Tablets U.S. Prescribing Information 2015



# Recorlev upcoming milestones projected timing

- Submit SONICS data for publication in a peer reviewed journal - Q3 2019
- Complete enrollment in LOGICS - early January 2020
- Announce LOGICS top-line primary endpoint results – end of Q1 2020 (~12 weeks from completion of enrollment)
- Submit the NDA for Recorlev – end of Q3 2020
- Initiate commercial readiness activities – on-going

# Keveyis

(dichlorphenamide)

The first and only FDA-approved therapy  
for primary periodic paralysis\*

\* FDA-approved treatment for hyperkalemic, hypokalemic, and related variants of primary periodic paralysis

# Primary periodic paralysis: a spectrum of rare, chronic, genetic, neuromuscular disorders

## PPP

Causes recurrent, progressive, and debilitating episodes of muscle weakness and temporary paralysis<sup>2-4</sup>

## Symptoms/triggers

Symptoms: clumsiness, extreme fatigue, weakness, palpitations, pain

Triggers: may include potassium, carbohydrates, rest after exercise, cold exposure, stress

## Impact of attacks

Paralytic attacks are acute episodes that can be debilitating<sup>4</sup>

Attacks may last from one hour to several days<sup>1</sup>

As patients age, muscle weakness can become permanent<sup>3</sup>

## Frequency

**59%**  
have **weekly**  
attacks

**28%**  
have **daily**  
attacks

# Keveyis approved for the treatment of PPP in the US

- The first and only FDA-approved therapy indicated for the treatment of primary hyperkalemic and hypokalemic periodic paralysis and related variants
- Twice-daily dosing in an oral tablet formulation
  - Starting dose is 50 mg 2X daily
  - Can be titrated up to 100 mg 2X daily
- ~4,000-5,000 diagnosed PPP patients in the United States \*

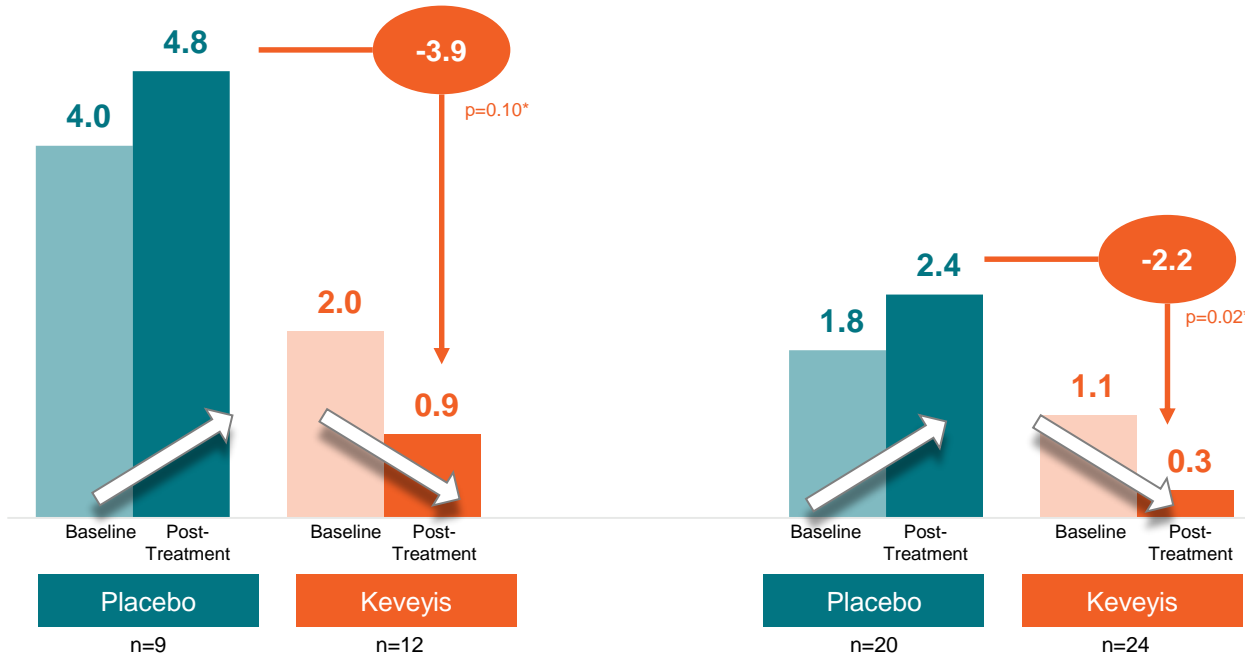
\* Based on Strongbridge analysis of medical claims database. Identified patients were required to have medical activity of any type in the last 12-36 months.

# Treatment with Keveyis decreased weekly attack rates

## Study 1: decreased weekly attack rates from baseline to week 9

Hyperkalemic

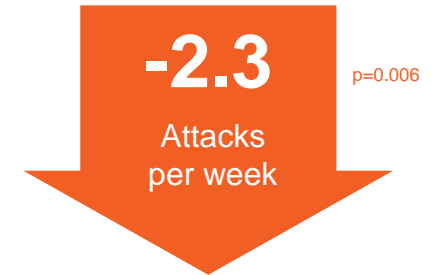
Hypokalemic



## Study 2

Hyperkalemic

Mean decrease in attack rates relative to placebo



Mean weekly attack rate at baseline was 3.8 (n=31)

Study 1: Sansone VA, et al. Neurology 2016;86:1408-1416  
Study 2: Tawil R, et al. Ann Nuerol. 2000; 47:46-53.

\*Treatment effects (DCP-placebo) are computed as the median of the bootstrap distribution of the treatment group difference in median response

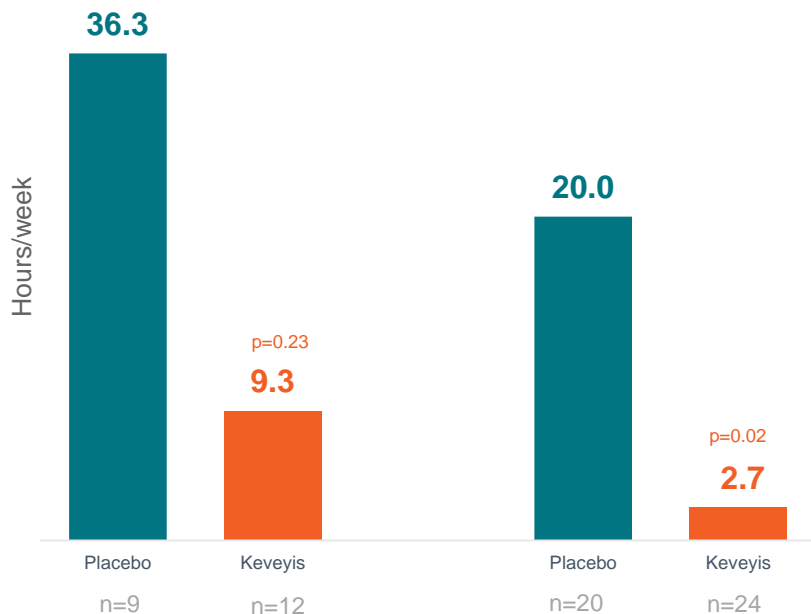
# Reduced duration of weekly attacks and decreased attack severity

Average values for each group over weeks 2-9

## Decreased weekly attack duration

Study 1: Hyperkalemic

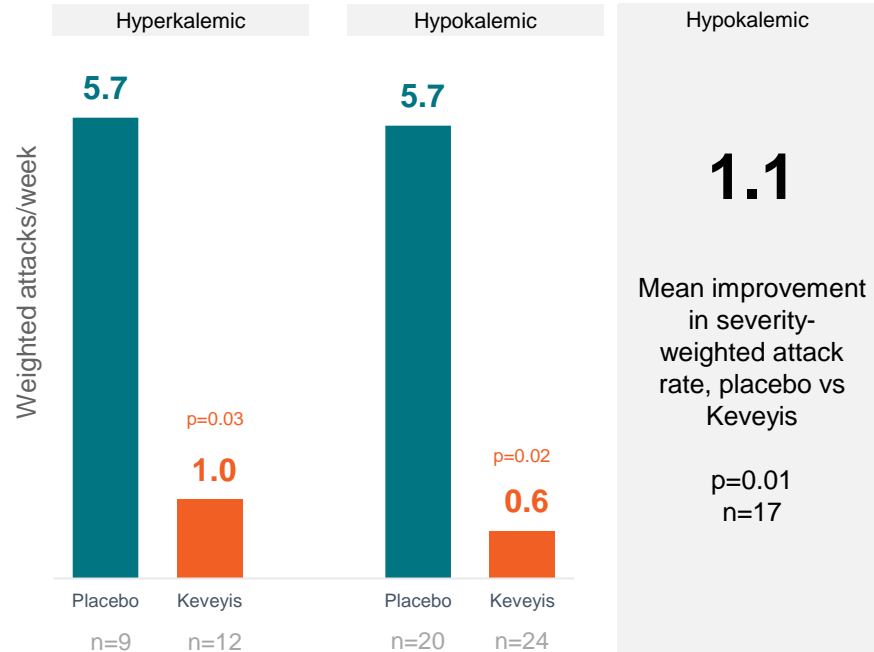
Study 1: Hypokalemic



## Decreased severity-weighted attack rate

Study 1

Study 2



Study 1: Sansone VA, et al. Neurology 2016;86:1408-1416  
Study 2: Tawil R, et al. Ann Nuerol. 2000; 47:46-53.

# Safety and tolerability

Adverse reactions ( $\geq 5\%$  and more common than in patients treated with placebo in Study 1)

	Adverse Reaction	Keveyis n=36 (%)	Placebo n=29 (%)
Nervous system disorders	Paresthesia	44	14
	Cognitive disorder	14	7
	Dysgeusia	14	0
	Confusional state	11	0
	Headache	8	7
	Hypoesthesia	8	0
	Lethargy	8	0
	Dizziness	6	0
Gastrointestinal disorders	Diarrhea	6	3
	Nausea	6	0
General disorders and administration site conditions	Fatigue	8	0
	Malaise	6	0
Investigations	Weight decreased	6	0
Musculoskeletal and connective tissue disorders	Muscle spasms	8	0
	Arthralgia	6	3
	Muscle twitching	6	0
Respiratory	Dyspnea	6	0
	Pharyngolaryngeal pain	6	0
Skin	Rash	8	0
	Pruritus	6	0

# Strategic priorities & revenue guidance

Continue to organize and construct the market

Focus commercial investment to accelerate pathway to profitability

Pursue life cycle opportunities to extend exclusivity runway beyond 2022

1H 2019 revenues: \$10.4M

Full year 2019 revenue guidance: \$18-20M



# IP & Financials

# Intellectual property and orphan exclusivity

	IP		Orphan exclusivity	
	US	EU	US	EU
Recorlev	<p>2030 Method of use: reducing CRP levels and systemic inflammation</p> <p>2026 Method of use: treating Cushing's syndrome</p>	<p>2026 Method of use: treating Cushing's syndrome</p>	<p>7 years</p>	<p>10 years</p>
Veldoreotide	<p>2037 Formulation</p>	<p>Filed patent application for novel formulation</p>	<p>7 years</p>	<p>10 years</p>
Keveyis	<p>Exploring options</p>	<p>US rights only</p>	<p>Aug 2022</p>	<p>US rights only</p>

# Financial Highlights (as of 6/30/2019)

- ~\$86.2 million in cash; no debt
- ~54.2 million shares outstanding
- 2019 Keveyis revenue guidance of \$18-20M
- Receiving funding of ~\$7-8 million per year from Novo Nordisk to support Strongbridge's 23-person rare endocrine commercial field organization
  - Funding for three years, beginning in December 2018

# Upcoming potential value drivers

## Recorlev

- Complete enrollment in LOGICS trial – early January 2019
- Report LOGICS primary endpoint top-line results – end of Q1 2020
- Planned NDA submission – end of Q3 2020

## Keveyis

- Drive revenue growth with focused financial resources
- On-track to achieve positive contribution margin - end of Q1 2020
- Pursue life cycle opportunities to extend exclusivity runway – update to market in 1H 2020

## Corporate

- Evaluate additional late-stage or commercial rare disease assets

# Strongbridge Biopharma plc

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