

Strongbridge Biopharma plc

June 2019

Forward-looking statements

This document contains forward-looking statements relating to the Company's strategy, objectives, business development plans and financial position. All statements other than statements of historical facts included in this document, including, without limitation, statements regarding the Company's future financial position, strategy, anticipated investments, costs and results, status and results of clinical trials, anticipated timing of release of results from clinical trials, size of patient population, potential advantages of a product or product candidate, discussion with regulators regarding the regulatory approval process for a product candidate, the release of additional planned analyses of clinical trials, plans, outcomes of product development efforts, intellectual property portfolio and objectives of management for future operations, may be deemed to be forward-looking statements. You can identify forward-looking statements by words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of those terms, and similar expressions that convey uncertainty or future events or outcomes.

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.

The forward-looking statements contained in this document are made only as of the date hereof. Except as otherwise required by law, the Company expressly disclaims any obligation or undertaking to release publicly any updates of any forward-looking statements contained in this document to reflect any change in its actual results, assumptions, expectations or any change in events, factors, conditions, or circumstances on which any forward-looking statement contained in this document is based.

Investment highlights

Revenue-Generating Rare Disease Company

Rare Endocrinology

Recorlev – Positive results from pivotal Phase 3 SONICS trial for Cushing’s syndrome; met primary endpoint at 6 months and favorable benefit-risk profile through 12 months

veldoreotide – preclinical reformulation of differentiated somatostatin analog, fully owned

Macrilen – Sold rights in December to Novo Nordisk for \$145M plus tiered royalties; Novo funding commercial endocrine field force for three years

Rare Neuromuscular

Keveyis – Only FDA-approved drug for all variants of Primary Periodic Paralysis

Established Commercial Infrastructure

Fully integrated commercial operations in two rare disease therapeutic areas



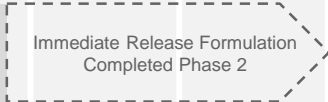


Effective Business Development

Proven ability to identify, evaluate and transact efficiently and effectively

Well Capitalized

- ~\$104M in cash and no debt as of 3/31/2019
- 2019 Keveyis revenue guidance of \$18-20M

Strongbridge and partnered product pipeline

		Indication/ Target Disease	Pre- clinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Rights
Rare Endocrinology	MACRILEN™ (macimorelin)	Adult Growth Hormone Deficiency diagnosis	Marketed					 US and Canada
	RECORLEV™ (levoketoconazole)	Endogenous Cushing's syndrome	Phase 3					 Global
	veldoreotide modified-release	Acromegaly, other 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	KEVEYIS® (dichlorphenamide)	Primary Periodic Paralysis	Marketed					 US

Upcoming potential value drivers

Recorlev

- Report LOGICS primary endpoint responder rate analysis top-line results by end of Q1 2020
- Planned NDA submission in Q3 2020

Keveyis

- Drive revenue growth with focused financial resources
- On track to achieve positive contribution margin by end of Q1 2020
- Pursue life cycle opportunities to extend exclusivity runway beyond 2022

Macrilen

- Maximize royalty income by collaborating commercially with Novo Nordisk to accelerate product uptake and growth

Corporate

- Evaluate additional late-stage or commercial rare disease assets

Recorlev

(levoketoconazole)

Cushing's syndrome complications and comorbidities

Cushing's 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



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:^{1*}

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

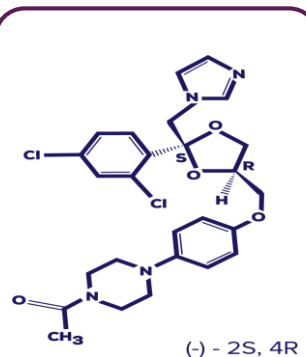
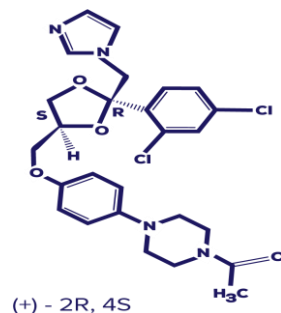
Source: Company sponsored research and published research including Feelders RA, Hofland LJ. (J Clin Endoc Metab. 2013;98(2):425-438) and Daly et al. (J Clin Endoc Metab 2006) *According to a retrospective analysis of claims from a large US commercial health plan (885 selected Cushing's disease cases and 2,655 matched controls without Cushing's disease) from 2007 to 2011. Burton T, et al. *Pituitary*. 2016;19:167–174. Geer et. al. (Endoc Pract 2017 Aug;23(8):962-970)

Recorlev (levoketoconazole) is the pure 2S,4R enantiomer of ketoconazole

KETOCONAZOLE

Two enantiomers combined

Not approved in the US to treat Cushing's syndrome



RECORLEV

Single enantiomer only (new chemical entity)

Single enantiomers often have significantly different clinical effects than their racemates

US/EU orphan designation for Cushing's syndrome

Development History and Regulatory Pathway

- Global phase 3 development program for Cushing's syndrome – positive SONICS results
 - Previously studied in two Phase 2 studies of diabetes (118 subjects received Recorlev)
- FDA 505(b)(2) regulatory approval pathway
 - Differentiated FDA 505(b)(2) drugs de-risk approval and have been successful in rare diseases (e.g., Korlym, Procysbi)

Recorlev Phase 3 clinical program



Open label; 94 patients enrolled; completed

DOSE TITRATION:
2 to 21 weeks

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

MAINTENANCE:
6 months

Maintain mUFC normalization with fixed therapeutic dose

EXTENDED EVALUATION:
6 months

Primary endpoint mUFC level measured

Both are pivotal trials to support FDA regulatory submission for approval



Randomized withdrawal; 54 randomized patient target

LEVOKETOCONAZOLE-NAÏVE-ONLY DOSE TITRATION:
14 to 19 weeks

SONICS-completers enter at Randomized Withdrawal

RANDOMIZED WITHDRAWAL:
(Active)

RANDOMIZED WITHDRAWAL:
(Placebo)

RESTORATION PHASE

Primary endpoint responder rate

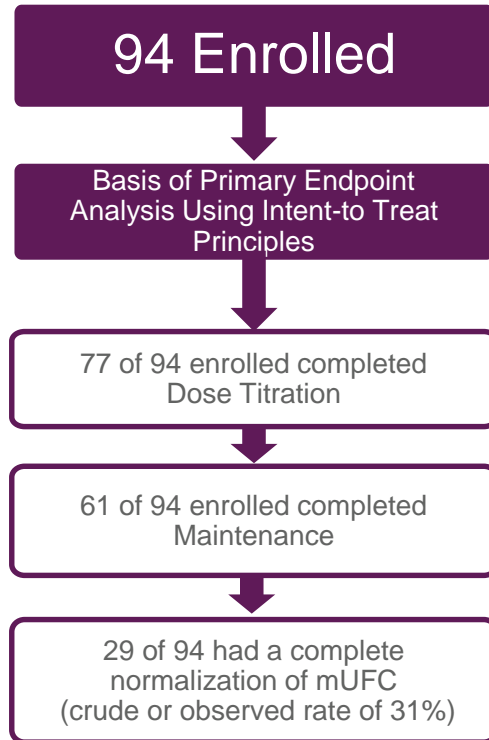


Open-label extension *

Up to 19 weeks

* OPTICS is not intended as pivotal trial

SONICS achieves statistical significance in primary and key secondary endpoints



Summary of Maintenance Phase Results (ITT)

- Primary endpoint achieved statistical significance
30% of patients achieved mUFC normalization without dose increase (95% CI: 21%, 40%; p=.0154)
- Six key cardiovascular secondary endpoints achieved statistical significance (p<.0001 for each)
- No unexpected safety signals; 13% discontinuation rate due to treatment-emergent adverse events

Secondary endpoint data support clinically meaningful improvements in cardiovascular risk markers

Outcome Measure at End of Maintenance Phase	Baseline Mean, (n)	Mean Change From Baseline†, (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

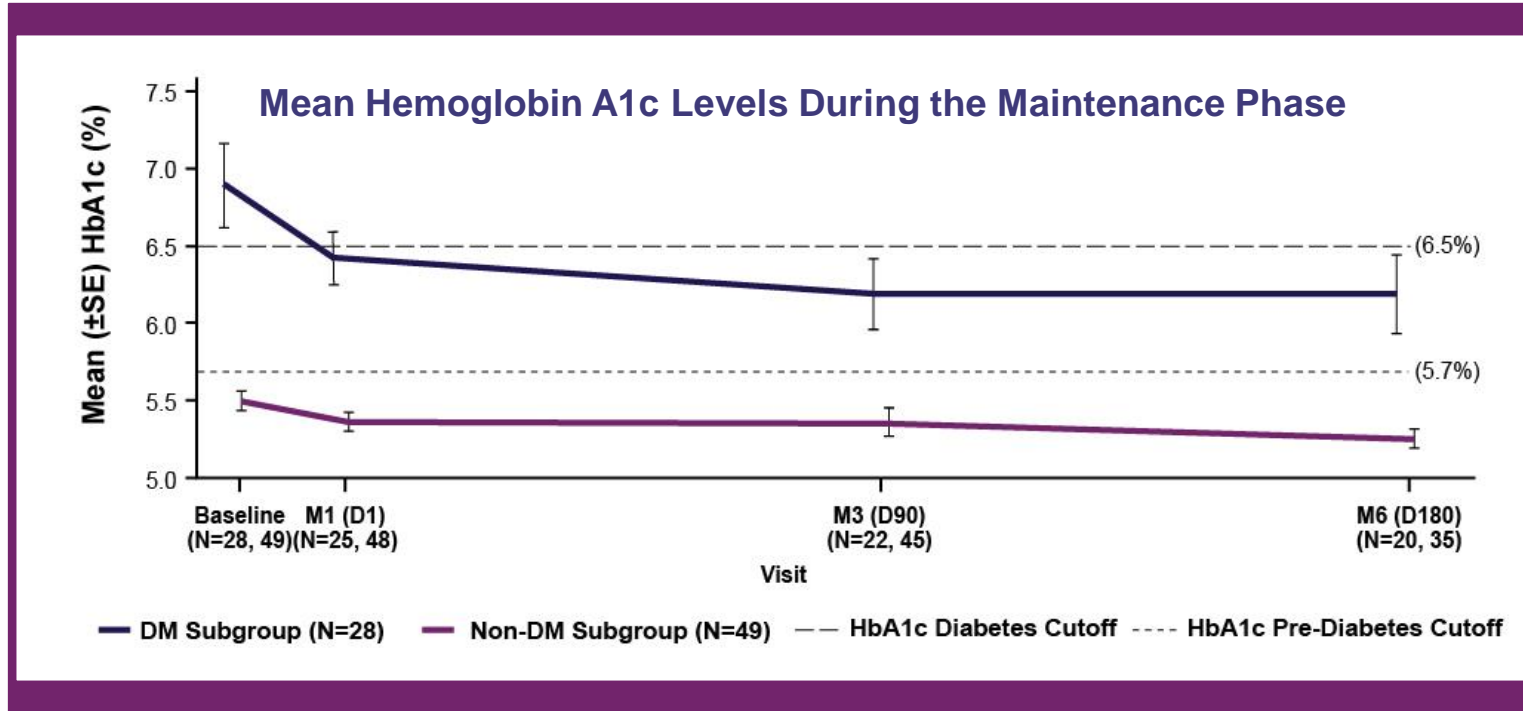
Extended evaluation phase (additional six months of maintenance therapy)

- Clinically meaningful improvements in key cardiovascular risk markers were observed through 12 months of maintenance therapy
 - Reductions from baseline in mean fasting glucose, hemoglobin A1C, and total and LDL-cholesterol
- Weight loss continued through the extended evaluation phase

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

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

Improvements in HbA1c after six months of maintenance therapy were more pronounced in patients with diabetes mellitus (DM)



Improvements in fasting blood glucose were also more pronounced among patients with diabetes mellitus (DM)

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)

Favorable liver safety findings after 12 months of maintenance therapy

	Recorlev	Signifor LAR*
ALT >3x ULN (includes those > 5x ULN)	10.6%	14%
ALT >5x ULN	3.2%	5%
Total bilirubin values > 1.5x ULN	0%	NA
Liver warning & precautions	TBD	Yes (but no black box)
	<p>SONICS Monitoring Protocol:</p> <p>At least once every two weeks during dose titration.</p> <p>Monitored monthly for six months after the therapeutic dose is established; then every three months thereafter.</p>	<p>Product Labeling:</p> <p>No boxed warning for liver safety.</p> <p>Monitor at least once prior to treatment and again after the first two-to-three weeks of treatment; then monthly for three months.</p>

11% 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

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

*Signifor LAR Prescribing Information

No unexpected adverse events

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

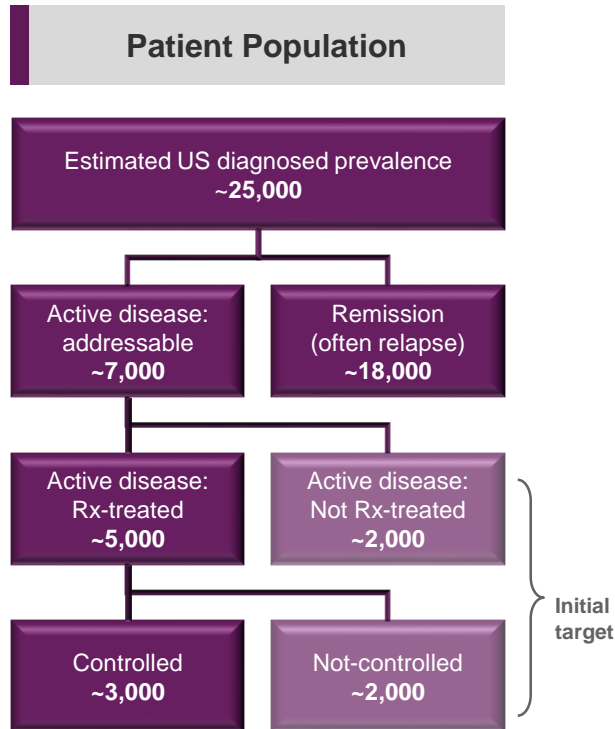
Adverse Event	% of enrolled (N=94)
Nausea	33%
Headache	29%
Peripheral edema	19%
Hypertension	19%
Fatigue	18%
ALT increased*	17%
Diarrhea	16%
Arthralgia	15%

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.

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

Indications	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...." ¹
Dosage and administration	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." ¹
Boxed warnings	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." ¹
Adverse reactions to unapproved uses	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." ¹

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

Recorlev upcoming milestones

- Submit Phase 3 SONICS data for publication in a peer reviewed journal in Q3 2019
- Announce top-line primary endpoint results for the LOGICS Phase 3 trial by the end of Q1 2020
- Submit the NDA for Recorlev in 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 paralysis²⁻⁴

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 debilitating⁴

Attacks may last from one hour to several days¹

As patients age, muscle weakness can become permanent³

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
- There are ~4,000-5,000 diagnosed PPP patients in the United States *

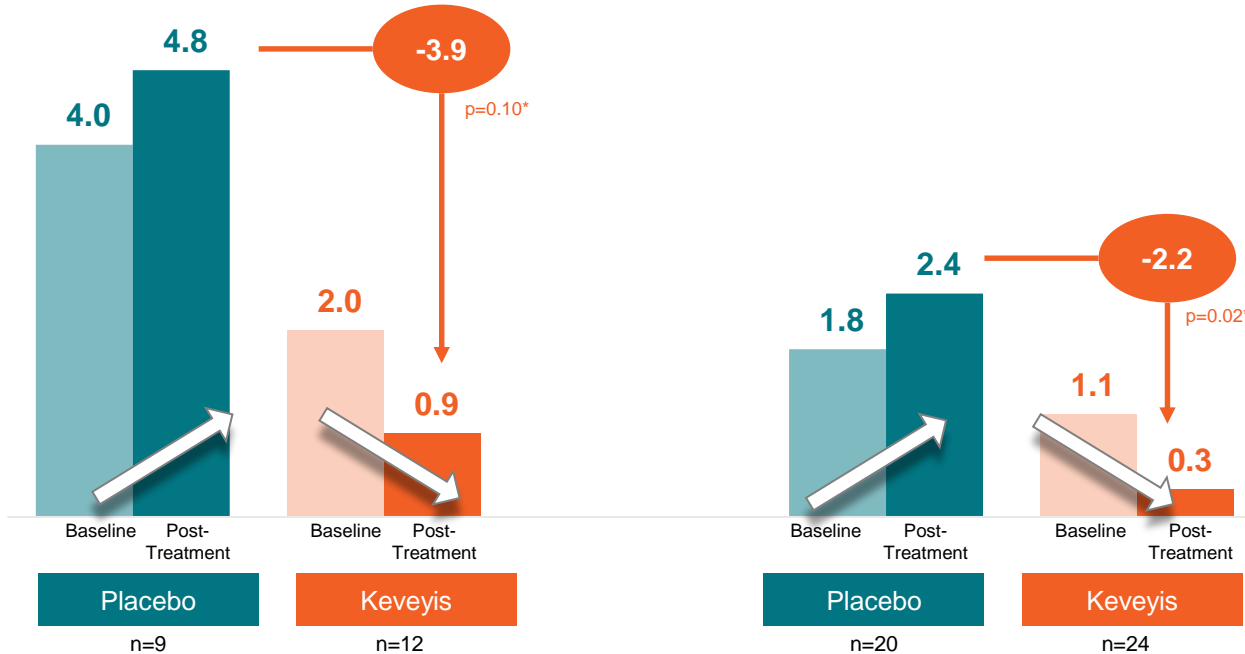
* Based on Strongbridge analysis of medical claims database. Identified patients were required to have medical activity of any type in the last 12-36 months.

Treatment with Keveyis decreased weekly attack rates

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

Hyperkalemic

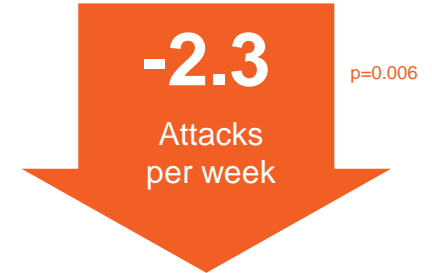
Hypokalemic



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

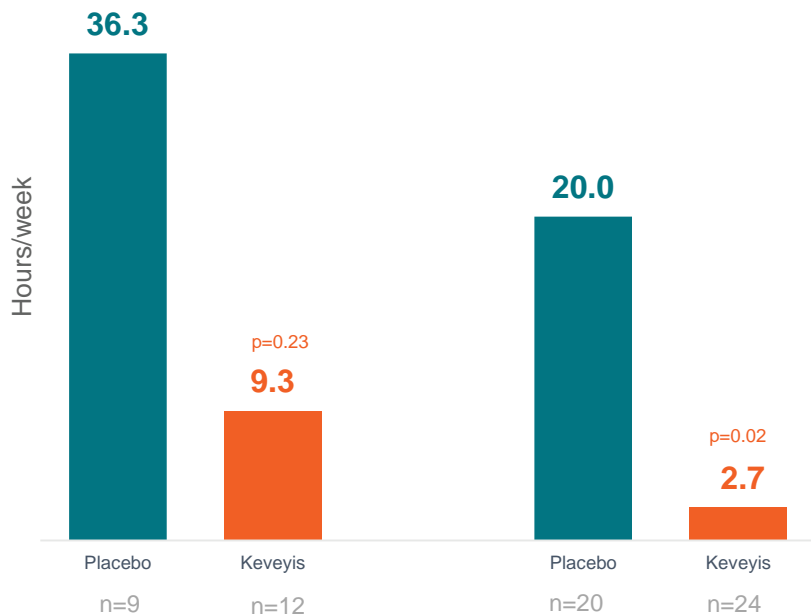
Reduced duration of weekly attacks and decreased attack severity

Average values for each group over weeks 2-9

Decreased weekly attack duration

Study 1: Hyperkalemic

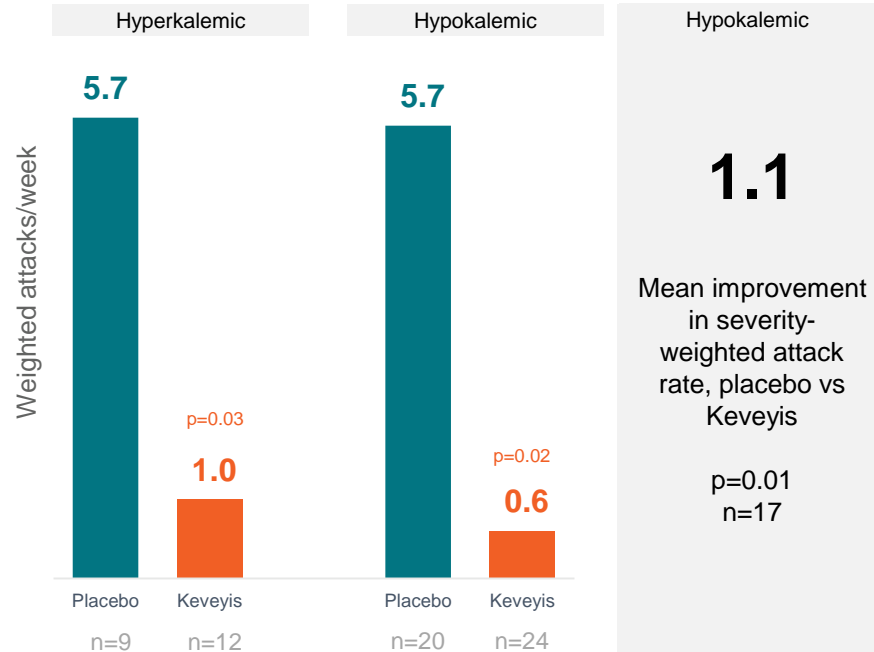
Study 1: Hypokalemic



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

Q1 2019 revenues: \$4.3M

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 3/31/2019)

- ~\$104 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

- Report LOGICS primary endpoint responder rate analysis top-line results by end of Q1 2020
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Keveyis

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- Evaluate additional late-stage or commercial rare disease assets