Strongbridge Biopharma plc

October 2019

STRONGBRIDGE BIOPHARMA

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.

Strongbridge portfolio

		Indication/ Target Disease	Pre-clinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Rights
Rare Endocrinology	RECORLEV™ (levoketoconazole)	Endogenous Cushing's syndrome	Phase 3					STRONGBRIDGE BIOPHARMA Global
Rare Endocrinology	veldoreotide modified-release	Conditions modifiable through activation of somatostatin receptors, such as Cushing's disease and neuroendocrine tumors	Pre-clinical	Immediate Release Formulation Completed Phase 2				STRONGBRIDGE BIOPHARMA Global
Rare Neuro-muscular	KEVEYIS® (dichlorphenamide)	Primary Periodic Paralysis	Marketed					STRONGBRIDGE BIOPHARMA US
Asset Sold	MACRILEN™ (macimorilen)	Adult Growth Hormone Deficiency diagnosis	Marketed					novo nordisk 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**
  - Positive Phase 3 SONICS Phase 3 trial results published in The Lancet Diabetes and Endocrinology
  - Anticipate LOGICS Phase 3 trial top-line results at end of Q1 2020
  - NDA submission planned for end of Q3 2020
- **Seasoned management team with strong business development capabilities**
  - Extensive experience in rare disease drug development and product launches
  - Proven ability to identify, evaluate and transact efficiently and effectively

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

Recorlev

(levoketoconazole)

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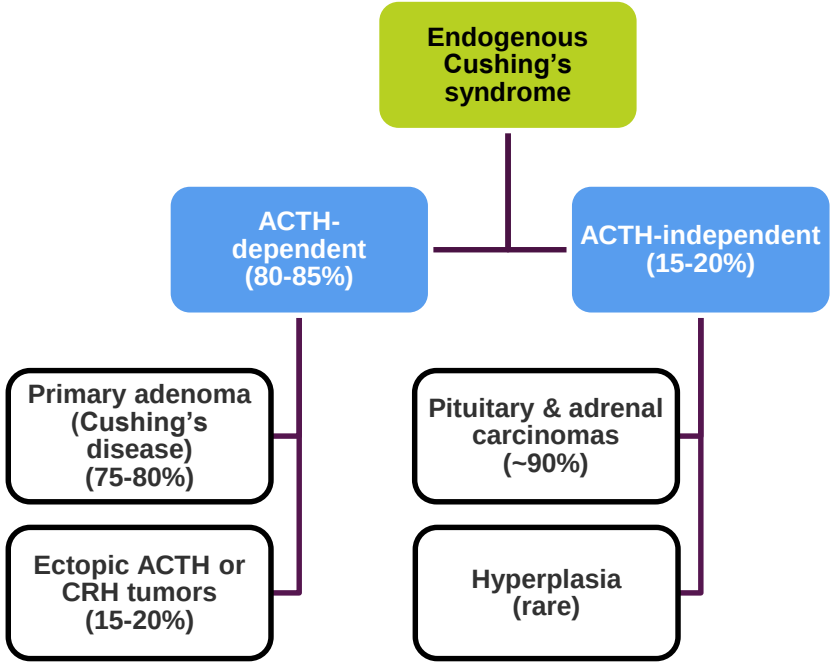
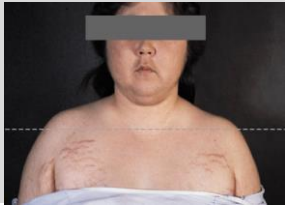
Endogenous Cushing syndrome overview

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



Abbreviation: ACTH, adrenocorticotropic hormone. CRH, corticotropin-releasing hormone

Source: Sharma TS, et al. Clin Epidemiol. 2015;7:281–293.

Cushing's syndrome unmet need and prevalence

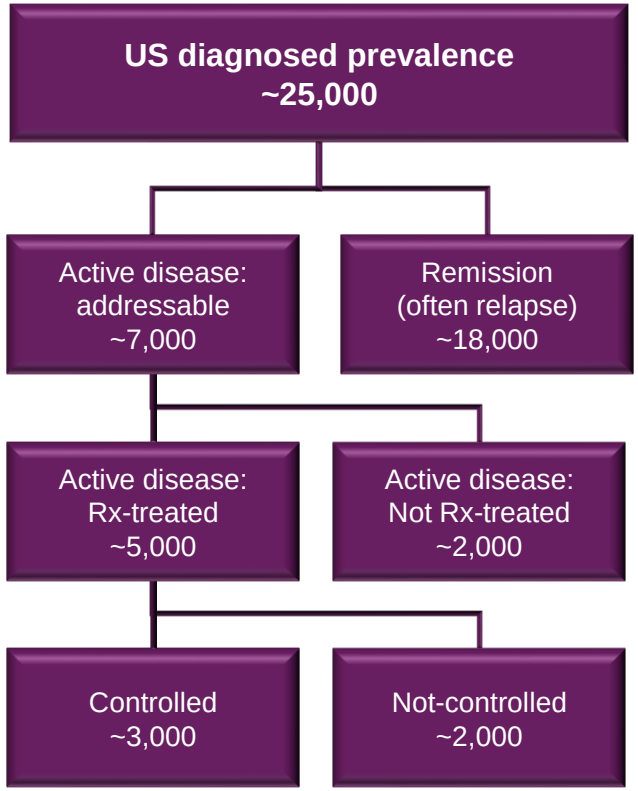
Unmet need and burden of illness

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:[1*]

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

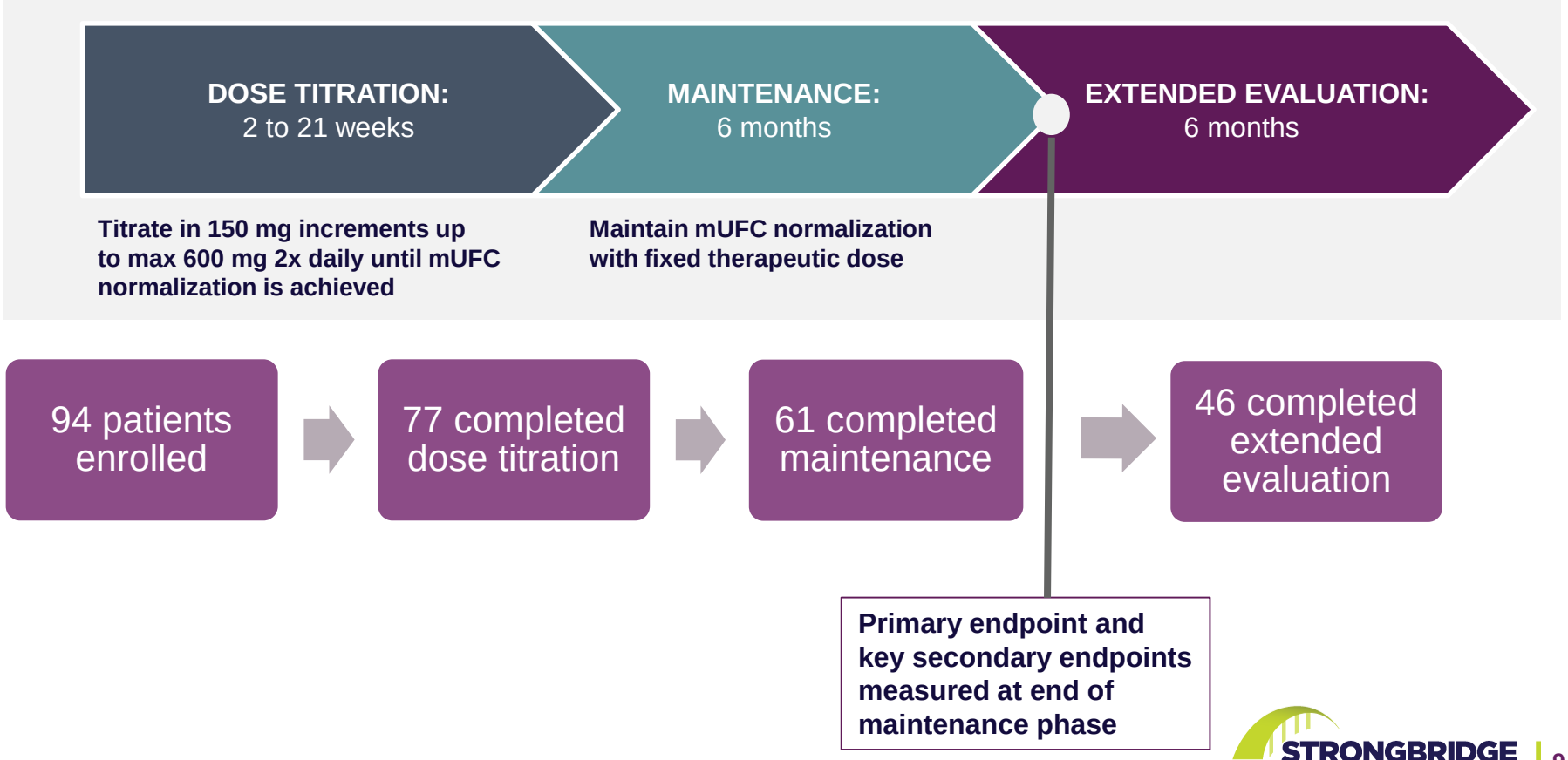


Source: Company sponsored research and published research including Feelders RA, Hofland LJ. (J Clin Endoc Metab. 2013;98(2):425-438) and Daly et al. (J Clin Endoc Metab 2006) *According to a retrospective analysis of claims from a large US commercial health plan (885 selected Cushing's disease cases 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) 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 is 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



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†, (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 ≥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 ≥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%

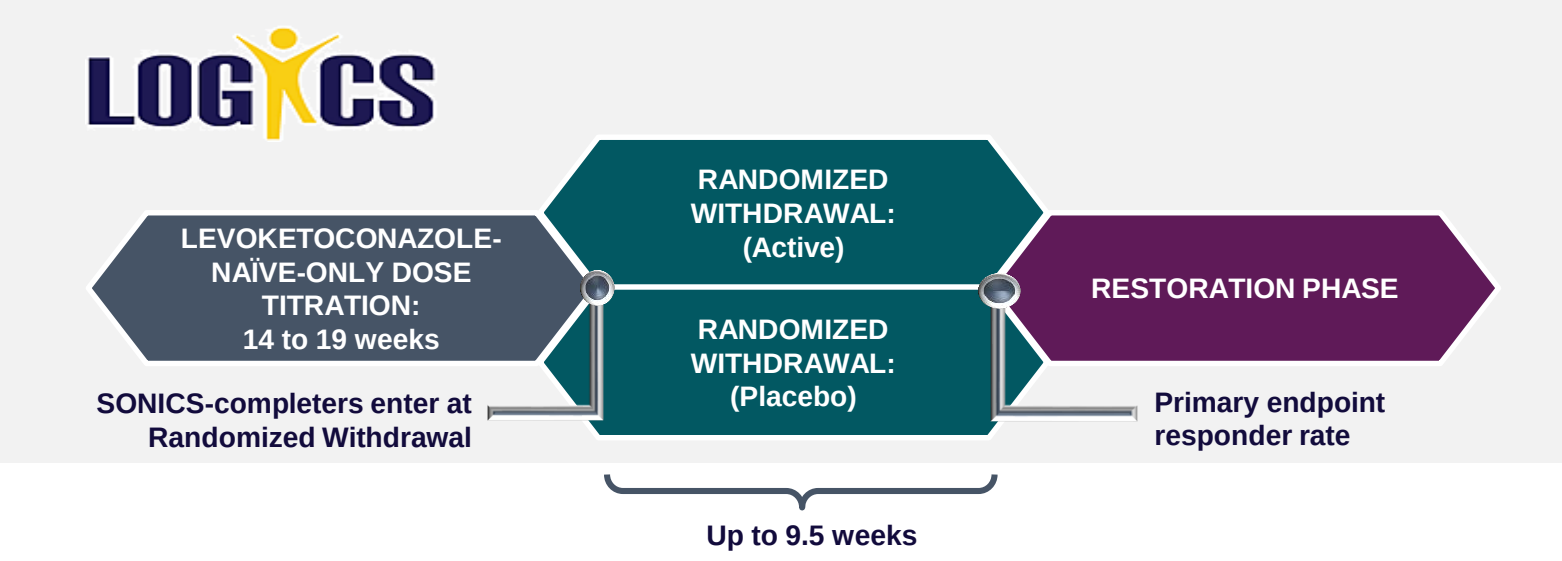
SONICS LFT Monitoring Protocol

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**

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

LOGICS Phase 3 placebo controlled trial

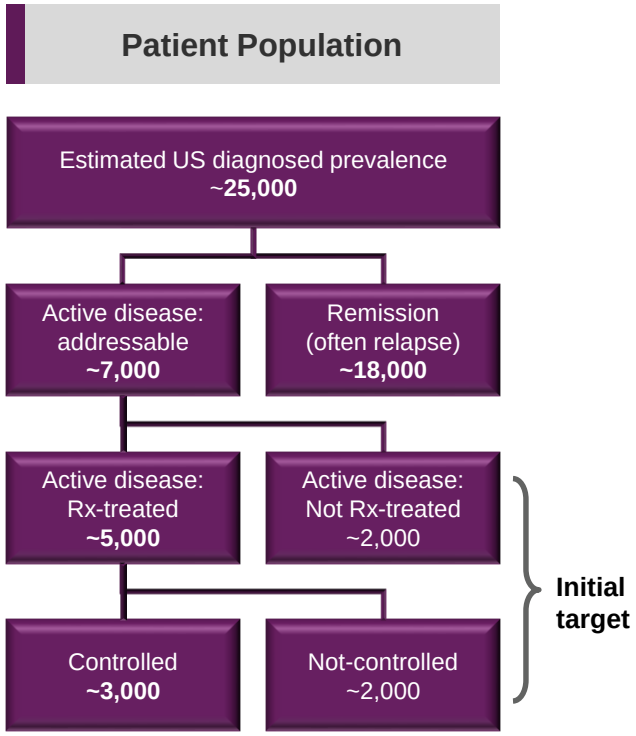


Enrollment - up to 54 patients

Primary endpoint - Comparison of the number of subjects with loss of therapeutic response upon withdrawing to placebo versus continuing treatment with levoketoconazole

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

Source: Company-sponsored research

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 projected timing

- 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

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

PPP	Symptoms/triggers	Impact of attacks	Frequency
Causes recurrent, progressive, and debilitating episodes of muscle weakness and temporary paralysis[2-4]	Symptoms: clumsiness, extreme fatigue, weakness, palpitations, pain Triggers: may include potassium, carbohydrates, rest after exercise, cold exposure, stress	Paralytic attacks are acute episodes that can be debilitating[4] Attacks may last from one hour to several days[1] As patients age, muscle weakness can become permanent[3]	**59%** have **weekly** attacks **28%** have **daily** attacks

Sources: 1. Charles G, Zheng C, Lehmann-Horn F, Jurkatt-Rott, Levitt J. Characterization of hyperkalemic periodic paralysis: a survey of genetically diagnosed individuals. *J Neurol*. 2013;260:2606-2613. 2. Cannon SC. Channelopathies of skeletal muscle excitability. *Compr Physiol.* 2015;5:761-790. 3. Cavel-Greant D, Lehmann-Horn F, Jurkat-Rott K. The impact of permanent muscle weakness on quality of life in periodic paralysis: a survey of 66 patients. *Acta Myol.* 2012;31:126-133. 4. Sansone V, Meola G, Links TP, Panzeri M, Rose MR. Treatment for periodic paralysis. *Cochrane Database Syst Rev.* 2008; Jan 23;(1):CD005045.

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

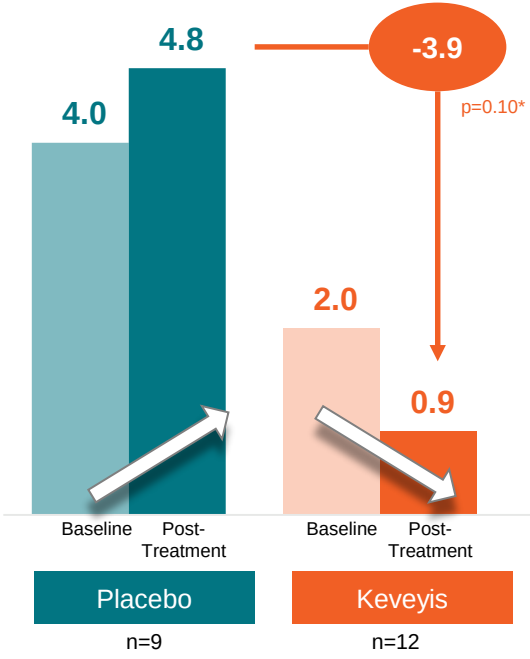
- ~4,000-5,000 diagnosed PPP patients in the United States *

* 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.

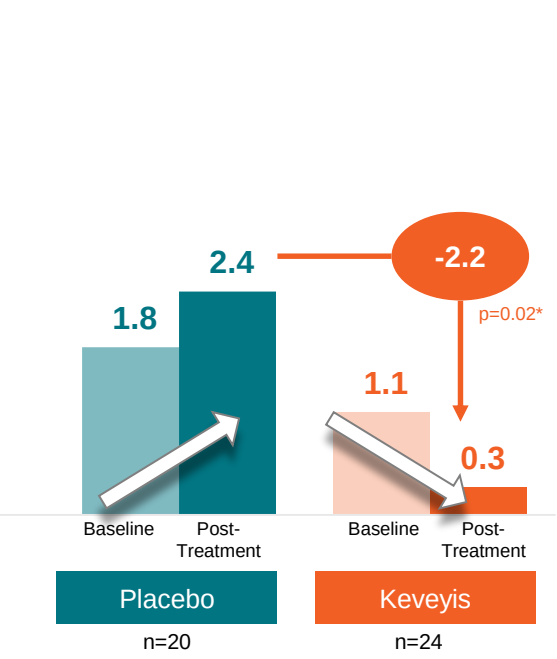
Treatment with Keveyis decreased weekly attack rates

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

Hyperkalemic



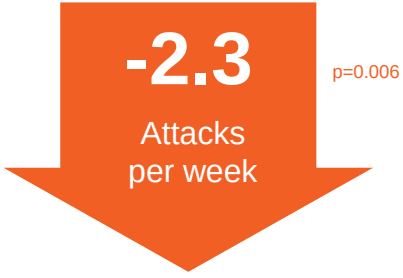
Hypokalemic



Study 2

Hyperkalemic

Mean decrease in attack rates relative to placebo



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

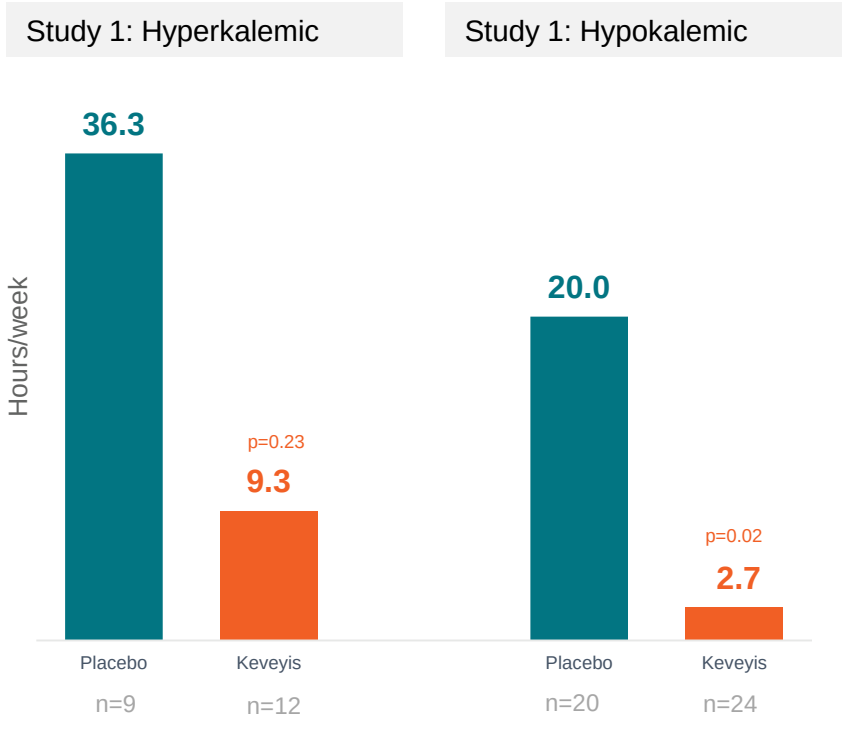
Study 1: Sansone VA, et al. Neurology 2016;86:1408-1416
Study 2: Tawil R, et al. Ann Nuerol. 2000; 47:46-53.

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

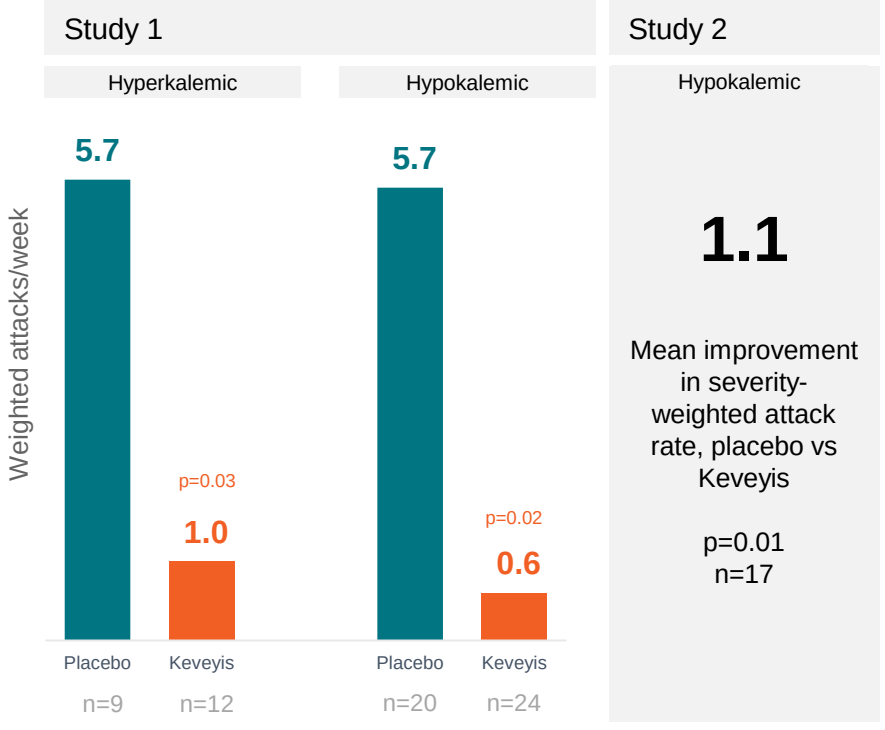
Reduced duration of weekly attacks and decreased attack severity

Average values for each group over weeks 2-9

Decreased weekly attack duration



Decreased severity-weighted attack rate



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

Secondary EPs in Study 1

Safety and tolerability

Adverse reactions (≥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

KEVEYIS prescribing information.

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

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Intellectual property and orphan exclusivity

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

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 2020 • 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

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