

Strongbridge Biopharma plc

January 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, size of patient population, potential advantages of a product or product candidate, discussion with regulators regarding the regulatory approval process for RECORLEV, the release of additional planned analyses of the SONICS study, 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

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

Recorlev – pivotal Phase 3 SONICS trial for Cushing's syndrome met primary endpoint

veldoreotide – preclinical reformulation of differentiated somatostatin analog, fully owned

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

Pro forma 9/30/18 cash and debt
(reflecting net proceeds from Novo Nordisk transactions and repayment of outstanding debt that occurred in December 2018)

- ~\$148M in cash; no debt

Strongbridge and partnered product pipeline

		Indication/ Target Disease	Pre-clinical	Phase 1	Phase 2	Phase 3	Marketed	Commercial Lead
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

Potential value drivers in 2019

Recorlev

- FDA Type C meeting (Q1 2019)
- LOGICS topline data (Q4 2019)
- SONICS data presentations (through H1 2019)

Keveyis

- Grow revenue-- continue to organize and construct the market
- Focus commercial investment
- Pursue life cycle opportunities to extend exclusivity runway beyond 2022

Macrilen

- Execute seamless transition of Macrilen to Novo Nordisk
- Maximize Strongbridge royalty income by collaborating commercially to accelerate growth

Corporate

- Evaluate additional late-stage or commercial rare disease assets

Macrilen

(macimorelin)

The first and only FDA-approved oral drug for
diagnosing adult growth hormone deficiency

Strategic rare endocrine transaction and collaboration with Novo Nordisk

DEAL TERMS	
Upfront Cash Payment	\$145 million from Novo Nordisk for U.S. and Canadian rights to Macrilen
Royalty	Strongbridge will receive tiered royalties related to sales of Macrilen through 2027: <ul style="list-style-type: none">• 2019-2021: 12% of annual net sales• 2022-2027: 4% of annual net sales up to \$100M plus 8% of net sales over \$100M
Strongbridge Endocrine Field Force	Novo Nordisk will leverage and fund Strongbridge's 23-person rare endocrine commercial field organization for up to three years (approximately \$7-\$8 million per year)
Equity Investment	Novo Nordisk purchased 5.2 million ordinary shares at a purchase price of \$7.00 per share

Recorlev

(levoketoconazole)

Cushing's syndrome complications and comorbidities

Cushing's syndrome symptoms



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

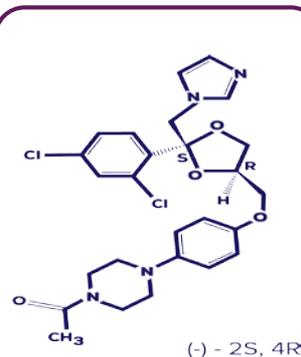
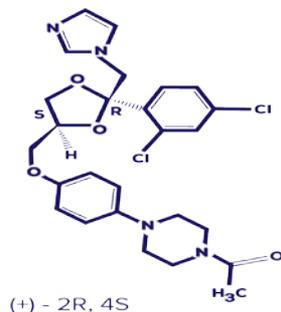
Source: Company sponsored research and published research including Feelders RA, Hofland LJ. (J Clin Endoc Metab. 2013;98(2):425-438) and Daly et al. (J Clin Endoc Metab 2006) *According to a retrospective analysis of claims from a large US commercial health plan (885 selected Cushing's disease cases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

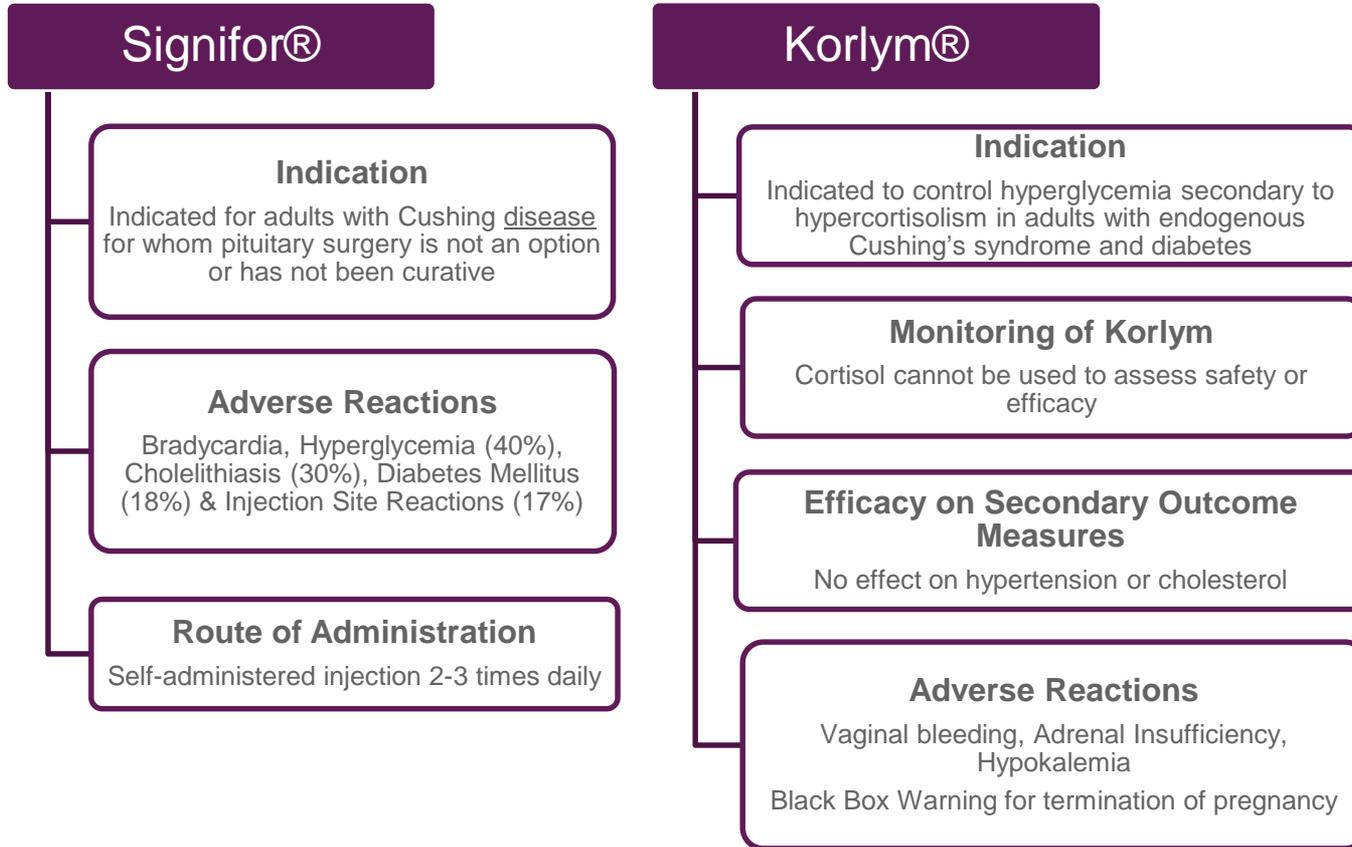
Ketoconazole labeled as last-line antifungal in U.S.

Includes warning against off label use in prostate cancer and Cushing's syndrome

Indications	Last-line anti-fungal, not indicated for Cushing's syndrome	"NIZORAL® (ketoconazole) Tablets should be used only when other effective antifungal therapy is not available or tolerated...NIZORAL 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 NIZORAL Tablets is a single daily administration of 200 mg (one tablet). If clinical responsiveness is insufficient within the expected time, the dose of NIZORAL 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 NIZORAL U.S. Prescribing Information 2014

Significant unmet need in Cushing's disease/syndrome



Phase 3 Recorlev clinical program



Open label; 94 patients enrolled



Both are pivotal trials to support FDA regulatory submission for approval



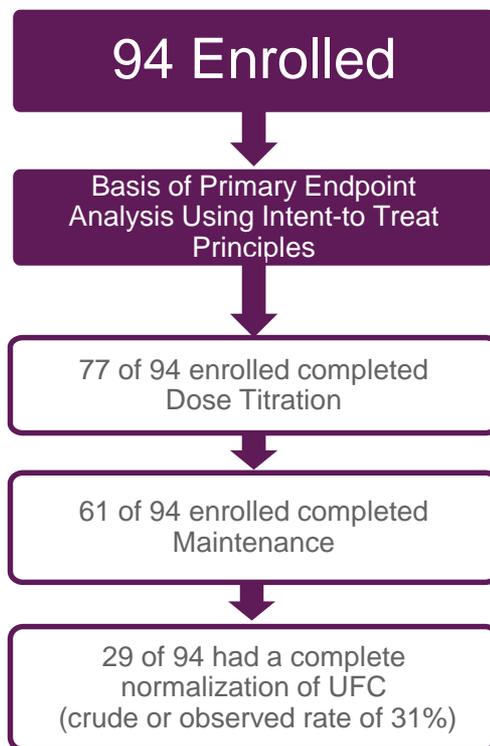
Randomized withdrawal; 54 randomized patient target



* OPTICS is not intended as pivotal trial

Up to 19 weeks

SONICS - Summary of Phase 3 Trial Results



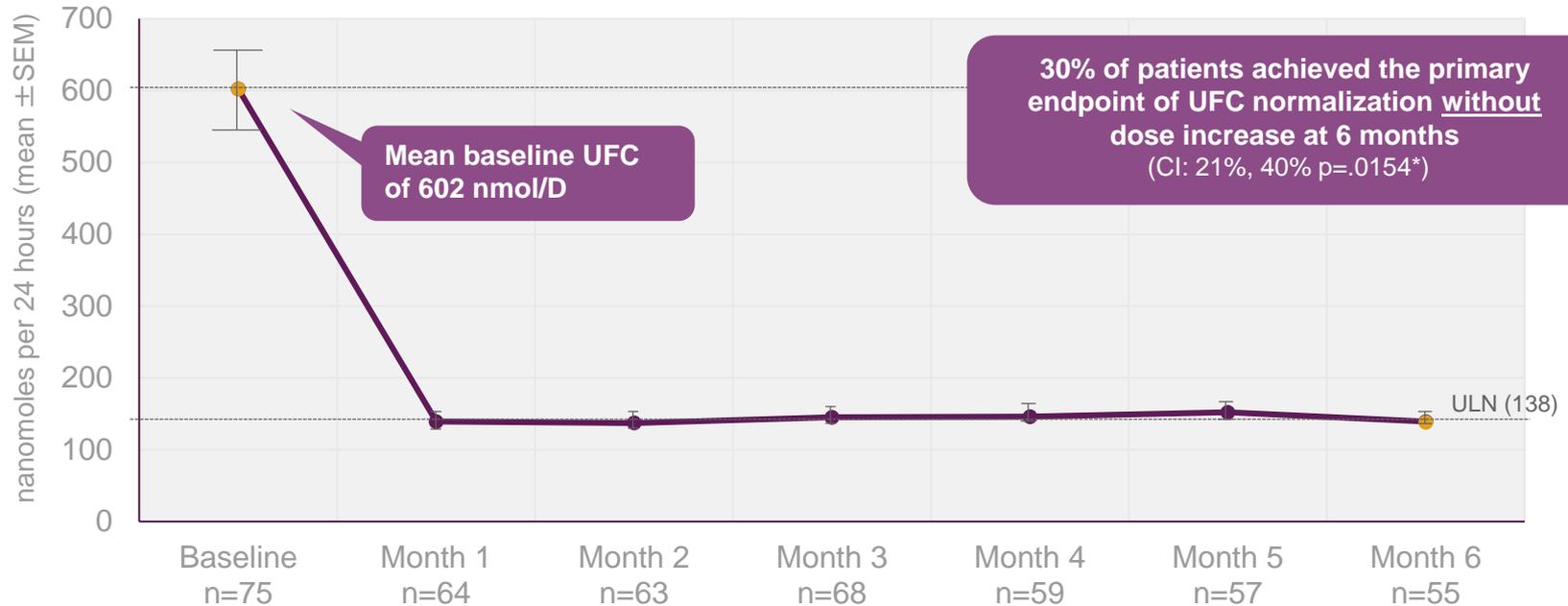
- **Primary endpoint achieved statistical significance**
30% of patients achieved UFC normalization without dose increase (95% CI: 21%, 40%; $p=.0154$)
- **Six key cardiovascular secondary endpoints achieved statistical significance** ($p<.0001$ for all)
- **Liver enzyme elevations**
11% of patients had liver enzyme elevation $>3x$ ULN on or before day 60 of maintenance; all reversible upon discontinuation without clinical sequelae
- **No unexpected safety signals**
13% discontinuation rate due to treatment-emergent adverse events

SONICS patient demographics

Baseline Characteristic	(N=94)
Age	44 years (mean) 18-75 years (range)
Sex	82% female, 49% with childbearing potential
Body Mass Index	29 kg/m ² (median)
Pituitary source of Hypercortisolism	85%
Diagnosis of Diabetes	38%
Diagnosis of Hypertension	71%
Diagnosis of Hypercholesterolemia	36%
Baseline UFC (multiple of ULN)	Median 3.0; Mean 4.9

SONICS trial achieved primary endpoint

Sustained reduction in mean UFC for six months after dose titration



* 1-sided vs. null hypothesis of 20% or lower rate

UFC Responder Analysis At End Of Maintenance Phase

	N=94
Primary endpoint of UFC normalization <u>without</u> dose increase	30%*, CI: 21%, 40% p=.0154
Sensitivity analysis of the primary endpoint (UFC normalization regardless of dose increase)	38%*†, CI: 28%, 49%
Analysis of observed rate at month 6 with imputation for missing UFC after month 3	42%‡, CI: 32%, 53%
≥50% UFC decrease or normalization, regardless of dose increase	48%*†, CI: 37%, 58%
Maintenance completers with UFC data and ≥50% UFC reduction from baseline	76% (42/55) **

* Analyses were based on mixed-effects, repeated measures model with an underlying binomial distribution and a logit link function and adjusting for baseline covariates. Estimates of the response and the associated the 95% Confidence Intervals (CIs) and the one-sided p-value (for the primary analysis only) are presented.

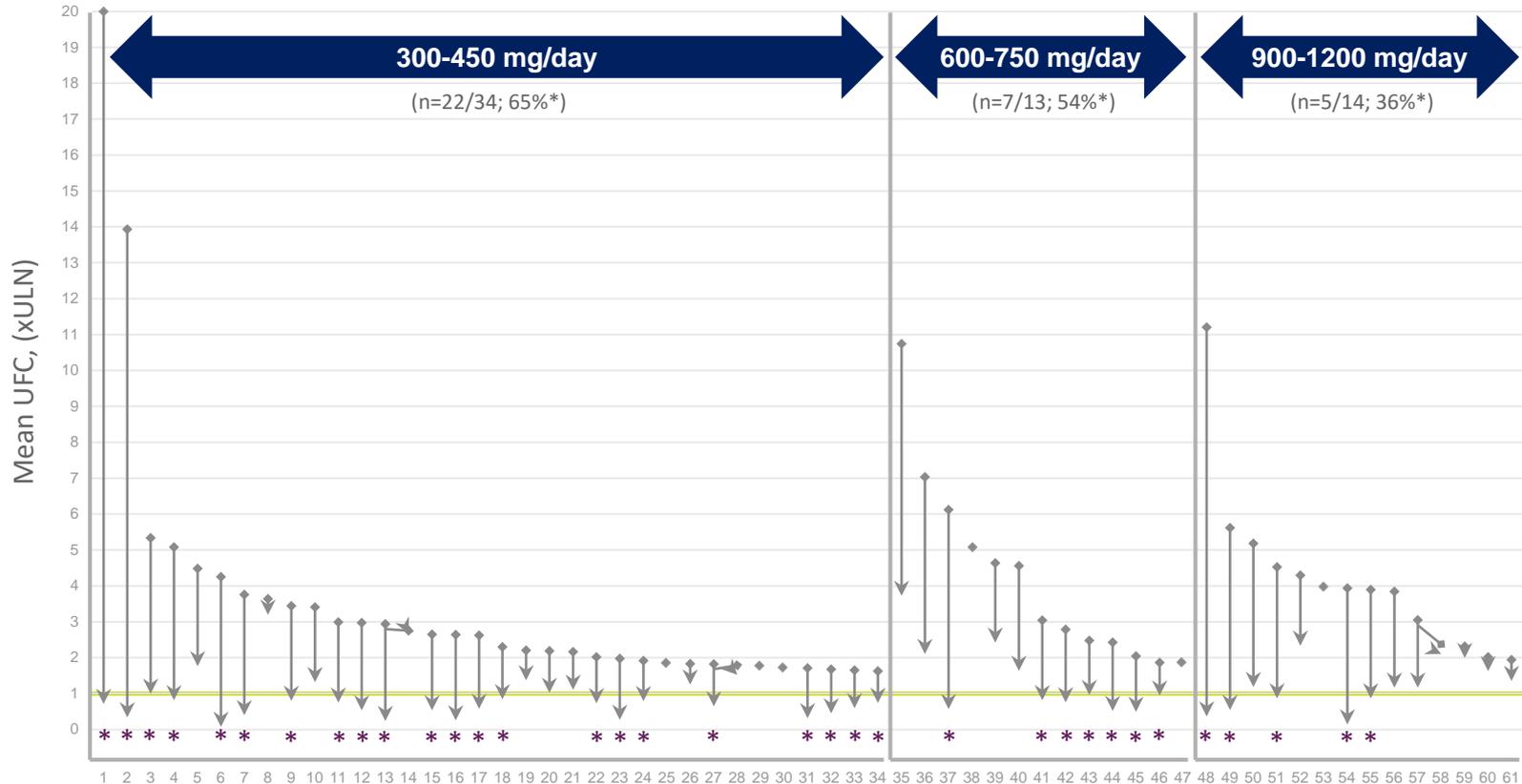
† This analysis had the additional imputation step of imputing normalization for missing a missing value at end of maintenance phase, if the subject also had normalization at the preceding and following visits.

‡ The CI is from the Clopper-Pearson two-sided 95% CI for the one-sample binomial proportion.

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

UFC response by patient for each patient who completed maintenance phase (n=61)

◆ Baseline
▼ 6 months



*Refers to proportion of subjects in each dose category achieving mUFC normalization in month 6 of maintenance phase regardless of need for dose increase.

SONICS achieved statistical significance in key secondary endpoints

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.

No statistically significant mean changes observed in blood pressure or c-reactive protein; small but statistically significant mean decrease observed in HDL-c.

Most commonly reported AEs ($\geq 15\%$, both phases combined)

Adverse Event	Subjects ≥ 1 AE	% of enrolled (N=94)
Nausea	30	32%
Headache	26	28%
Peripheral edema	18	19%
Hypertension	16	17%
Fatigue	15	16%
Diarrhea	14	15%
ALT increased*	14	15%

*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.

Adverse Events of Special Interest

Liver-related (7%)

QTc prolongation (5%)

Adrenal insufficiency (3%)

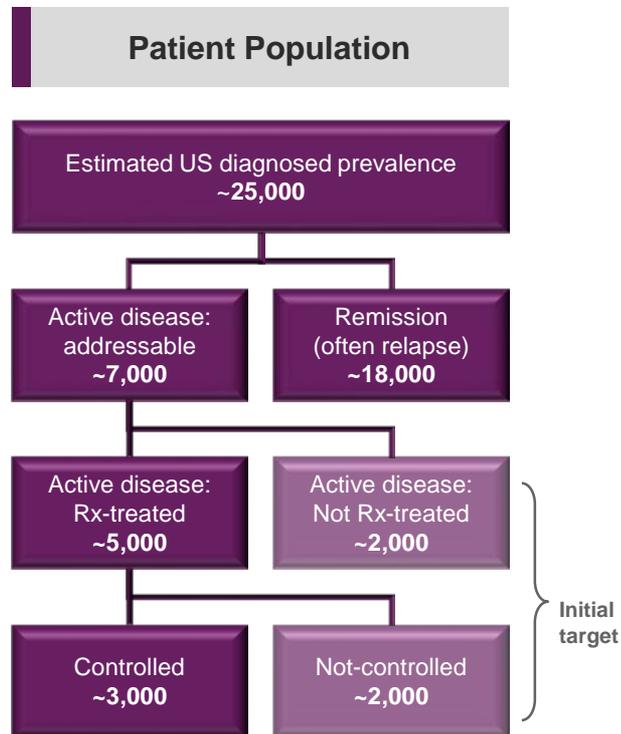
Liver safety findings

	Recorlev
ALT >3X ULN (includes those > 5x ULN)	10.6%
ALT >5x ULN	3.2%
Total bilirubin values > 1.5x ULN	0%
Liver warning & precautions	TBD
	<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>

	Signifor LAR*
	14%
	5%
	NA
	Yes (but no black box)
	<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>

* Signifor LAR Prescribing Information

Recorlev U.S. Commercial Opportunity



- SONICS data may support Recorlev launch strategy of positioning for both:
 - Drug-naïve patients, as first-line drug treatment
 - 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-\$400K 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)
- Ongoing Macrilen / endocrinology presence may accelerate Recorlev time to peak penetration

Recorlev upcoming milestones

- Type C meeting to discuss NDA filing strategy by end of Q1 2019
- Additional SONICS data to be reported at upcoming medical meetings
 - Pituitary Society – March 20-22, 2019
 - Endocrine Society – March 23-26, 2019
 - AACE – April 24-28, 2019
- SONICS top-line, one-year open label safety and tolerability data expected H1 2019
- LOGICS top-line data expected Q4 2019

Veldoreotide Extended Release

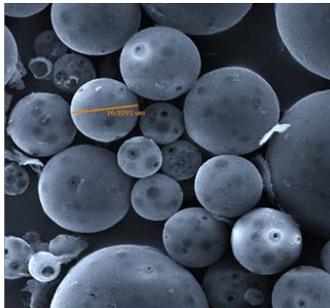
Veldoreotide History and Next Steps

2015-2018

Created long-acting formulation, generated IP resulting in new U.S. patent issuance in Aug 2018, and confirmed somatostatin receptor (SST) differentiation

2019-2020

Exploratory non-clinical work aimed at shaping clinical strategy



PLGA
microspheres

SST	Inhibition of	Octreotide	Lanreotide	Pasireotide	veldoreotide
1		Low / No	Low / No	High	Low / No
2	GH, Glucagon, Gastric acid	Very High	Very High	High	High
3		High	Medium	High	Low / No
4	GH	Low / No	Low / No	Low / No	High
5	GH, Insulin, Amylase	High	High	Very High	High

IC50 Range (nmol/l)	Very High	High	Medium	Low/No
	< 1	1 - 10	10 - 100	100 +

Adapted from data in M Afargan et al, Endocrinology Vol. 142 (2000); Y Patel, Frontiers in Neuroendocrinology 20, 157-198 (1999); I Shimon et al, J. Clin. Invest. Vol. 100, No. 9 (Nov. 1997); H Schmid et al., J. Endocrinology (2012) 212, 483-490

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

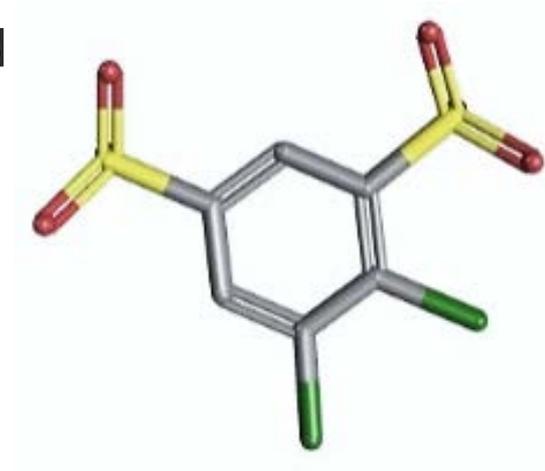
Estimated 4,000 – 5,000 diagnosed U.S. patients



* 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.

Keveyis Overview

- Strongbridge acquired U.S. rights to Keveyis[®] (dichlorphenamide) in December 2016 and launched in April 2017
- Keveyis is the **first and only** FDA-approved therapy indicated for the treatment of:
 - Primary hyperkalemic periodic paralysis
 - Primary hypokalemic periodic paralysis
 - 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

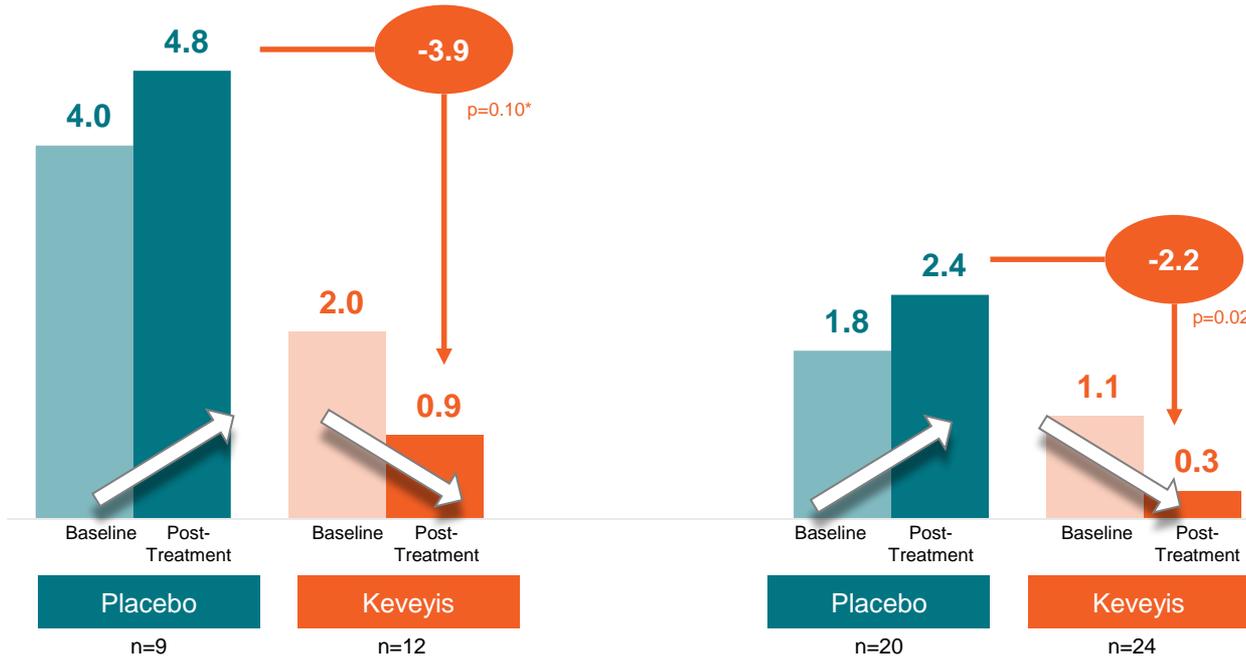


Treatment With Keveyis Decreased Weekly Attack Rates

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

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

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

YTD revenues through 09/30/2018: \$12.4M
2018 revenue guidance: \$16-17M

Intellectual property and orphan exclusivity

	IP		Orphan exclusivity	
	US	EU	US	EU
Macrilen	<p>2022 Composition of Matter</p> <p>2027 Method of use</p>	US and Canadian rights only	Dec 2024	US and Canadian rights only
Recorlev	<p>2030 Method of use: reducing CRP levels and systemic inflammation</p> <p>2026 Method of use: treating Cushing's syndrome</p>	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

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