

Strongbridge Biopharma plc

April 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 – Recent 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

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



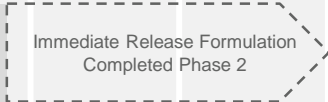


Effective Business Development

Proven ability to identify, evaluate and transact efficiently and effectively

Well Capitalized

- ~\$122M in cash; no debt (as of 12/31/2018)

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

- Regulatory update on NDA filing strategy (Q2 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 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

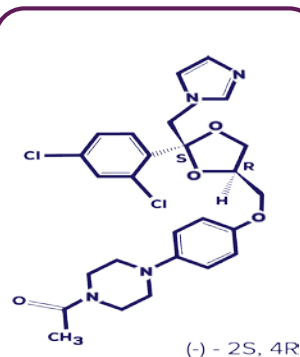
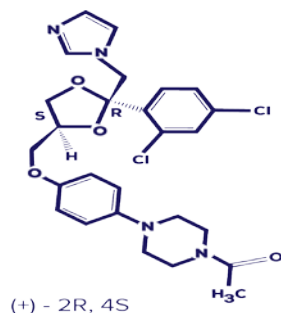
Source: Company sponsored research and published research including Feelders RA, Hofland LJ. (J Clin Endoc Metab. 2013;98(2):425-438) and Daly et al. (J Clin Endoc Metab 2006) *According to a retrospective analysis of claims from a large US commercial health plan (885 selected Cushing's disease cases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

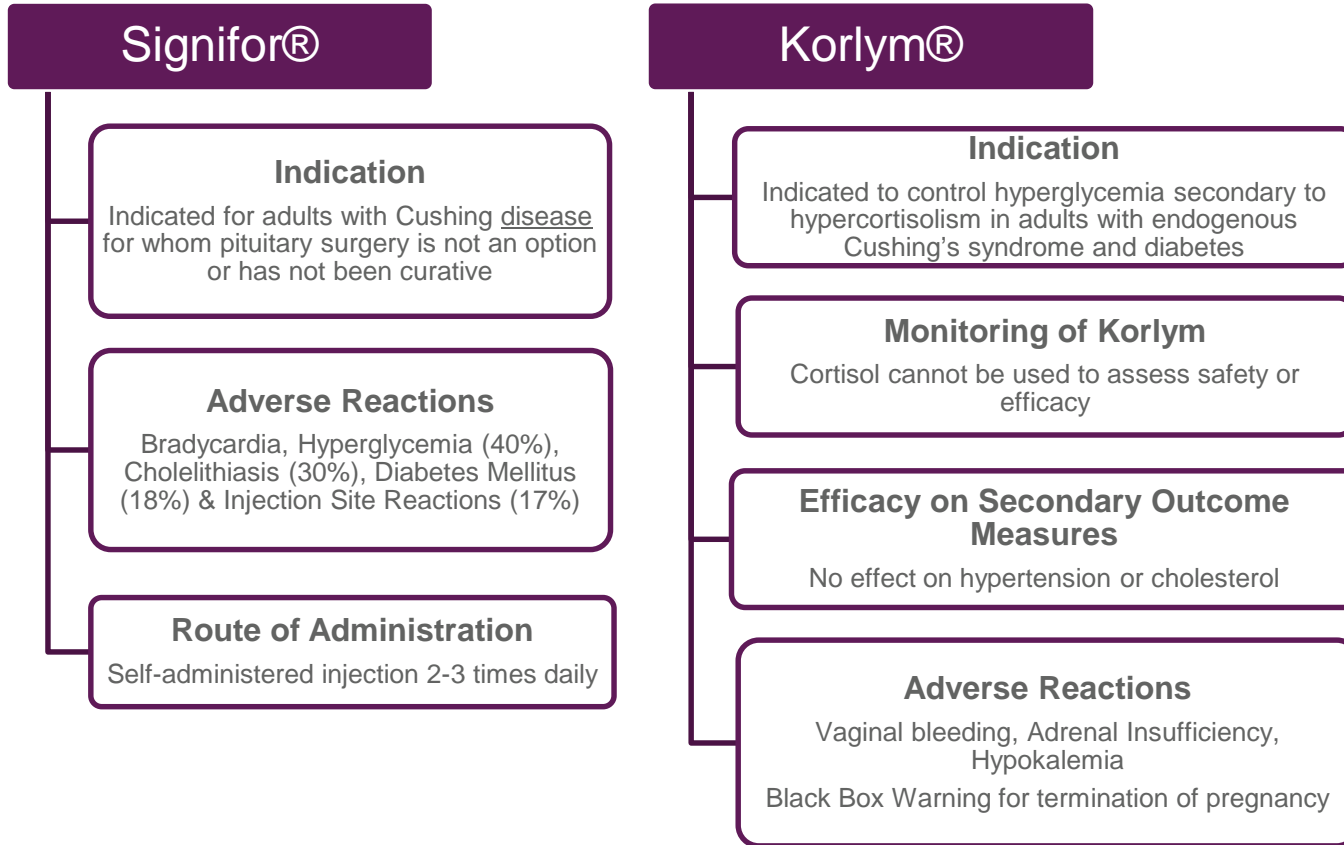
- Global phase 3 development program for Cushing's syndrome – positive SONICS results
 - Previously studied in two Phase 2 studies of diabetes (118 subjects received Recorlev)
- FDA 505(b)(2) regulatory approval pathway
 - Differentiated FDA 505(b)(2) drugs de-risk approval and have been successful in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

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

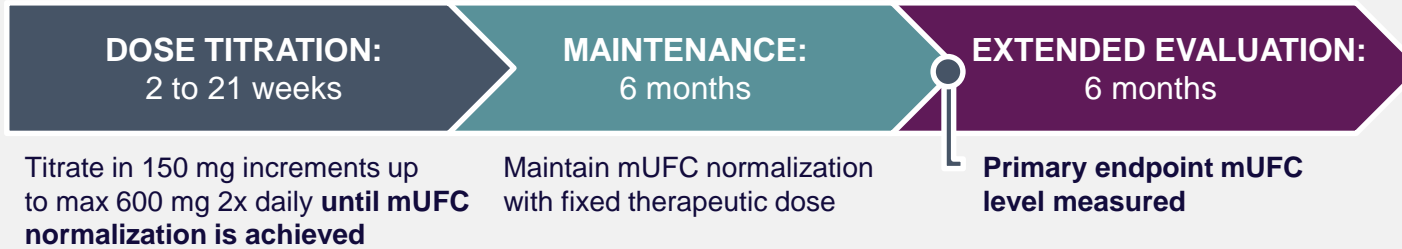
Significant unmet needs remain in Cushing's disease/syndrome despite approved medical treatments



Phase 3 Recorlev clinical program



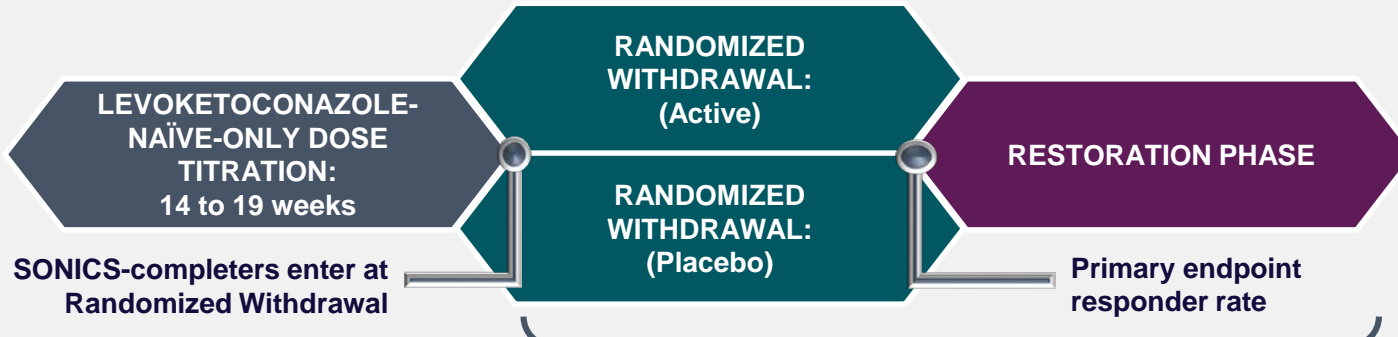
Open label; 94 patients enrolled; completed



Both are pivotal trials to support FDA regulatory submission for approval



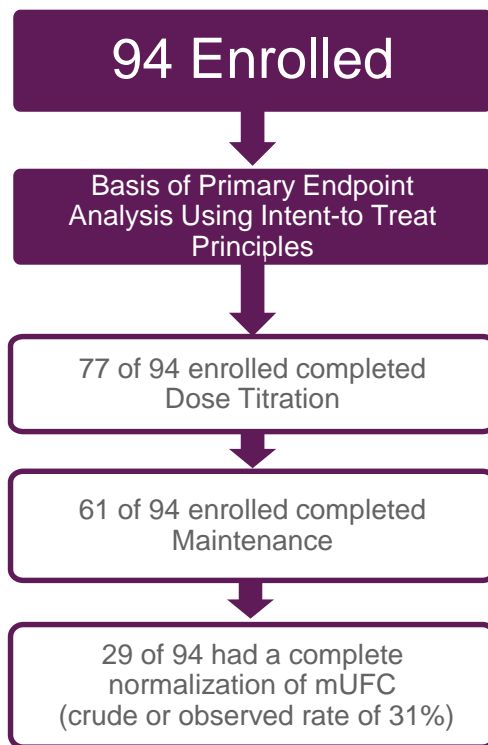
Randomized withdrawal; 54 randomized patient target



* OPTICS is not intended as pivotal trial

Up to 19 weeks

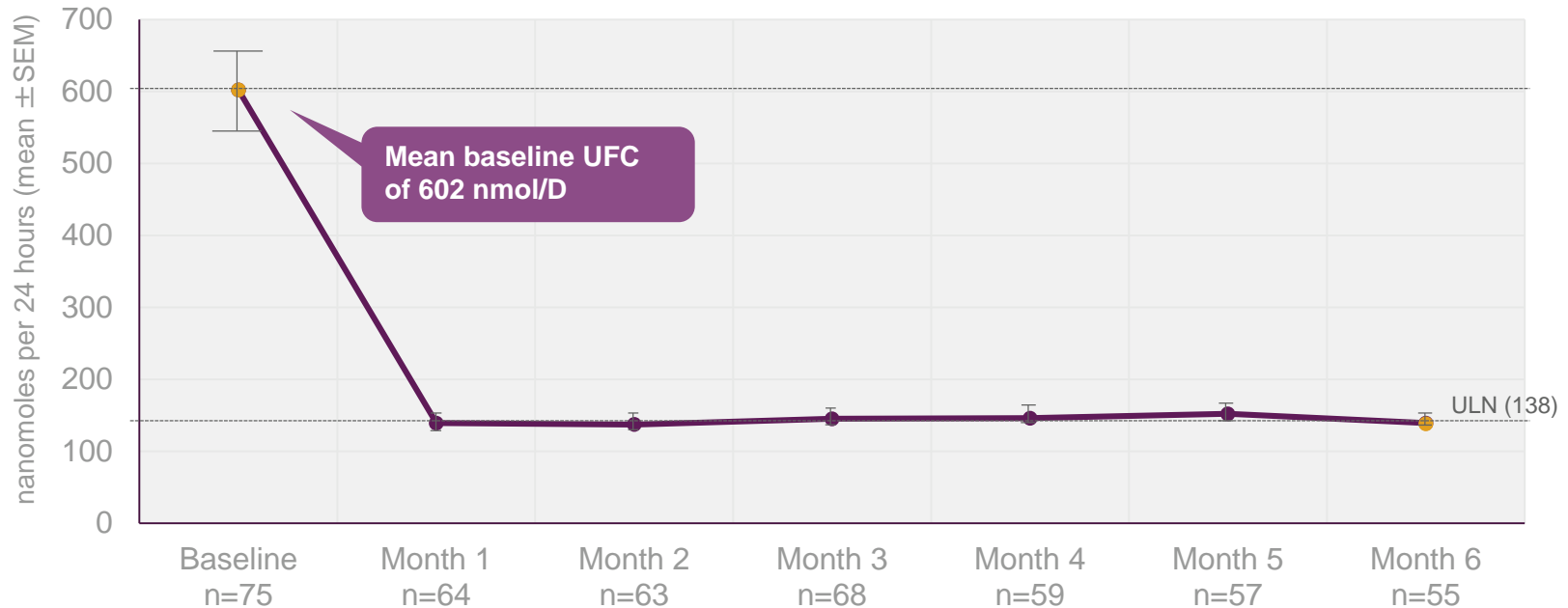
SONICS - Summary of Maintenance Phase Results



- **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 all)
- **No unexpected safety signals**
13% discontinuation rate due to treatment-emergent adverse events

SONICS trial achieved primary endpoint

Sustained reduction in mean UFC for six months after dose titration



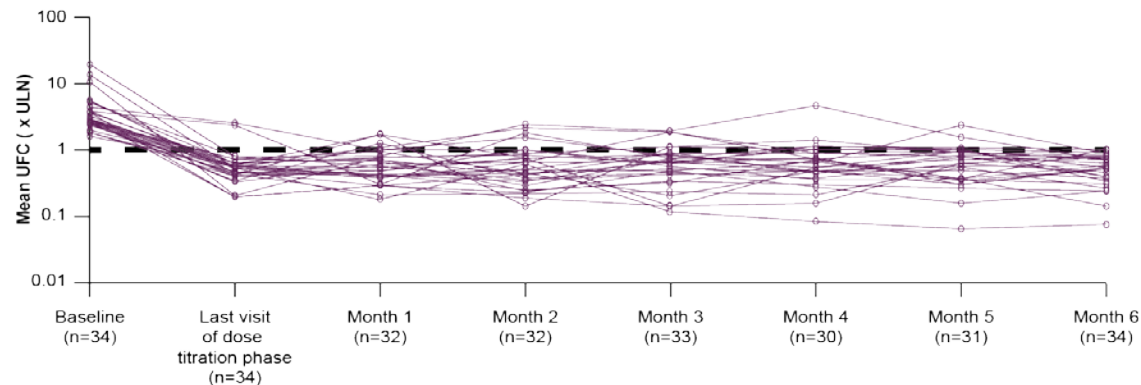
* 1-sided vs. null hypothesis of 20% or lower rate

Responder comparison after six months of maintenance therapy

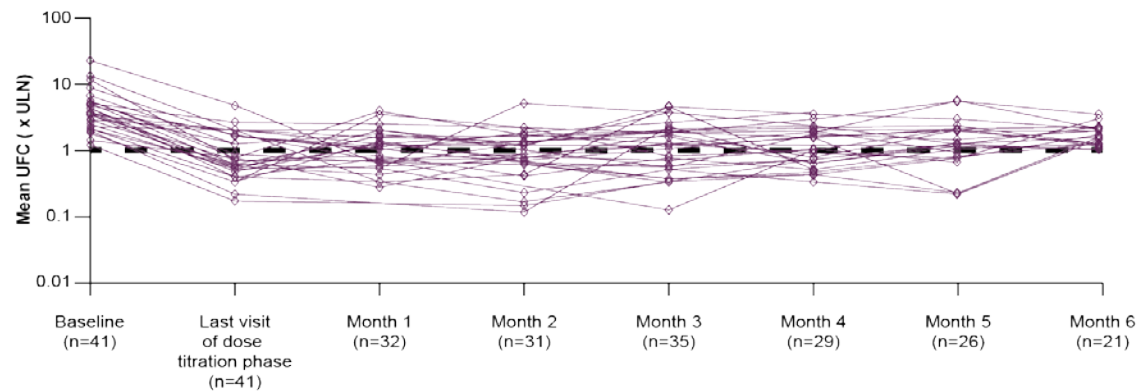
Individual line plots of mUFC (× ULN)

- More patients in the non-responder group had an initial response to treatment that left mUFC >ULN compared with the complete responder group, whereas the groups had relatively similar maintenance of their initial mUFC response over time

A. Complete Responders* (regardless of dose increase; n=34)



B. Non-Responders† (regardless of dose increase; n=41)



Two patients had no non-missing mUFC in the maintenance phase. They were considered as non-responders but are not represented in this figure. The dashed line represents the ULN for urinary free cortisol (138 nmol/24 hours [50 µg/24 hours]).

*Complete response defined as mUFC ≤ULN at EoM without a dose increase.

†Non-response: mUFC >ULN at EoM.

EoM = end of maintenance; mUFC = mean urinary free cortisol; ULN = upper limit of normal.

mUFC responder analysis after six and twelve months of maintenance therapy

	End of 6-Month Maintenance Phase	End of Extended Evaluation Phase (Additional 6 months of maintenance therapy)
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)

SONICS achieved statistical significance in key secondary endpoints after six months of maintenance therapy

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

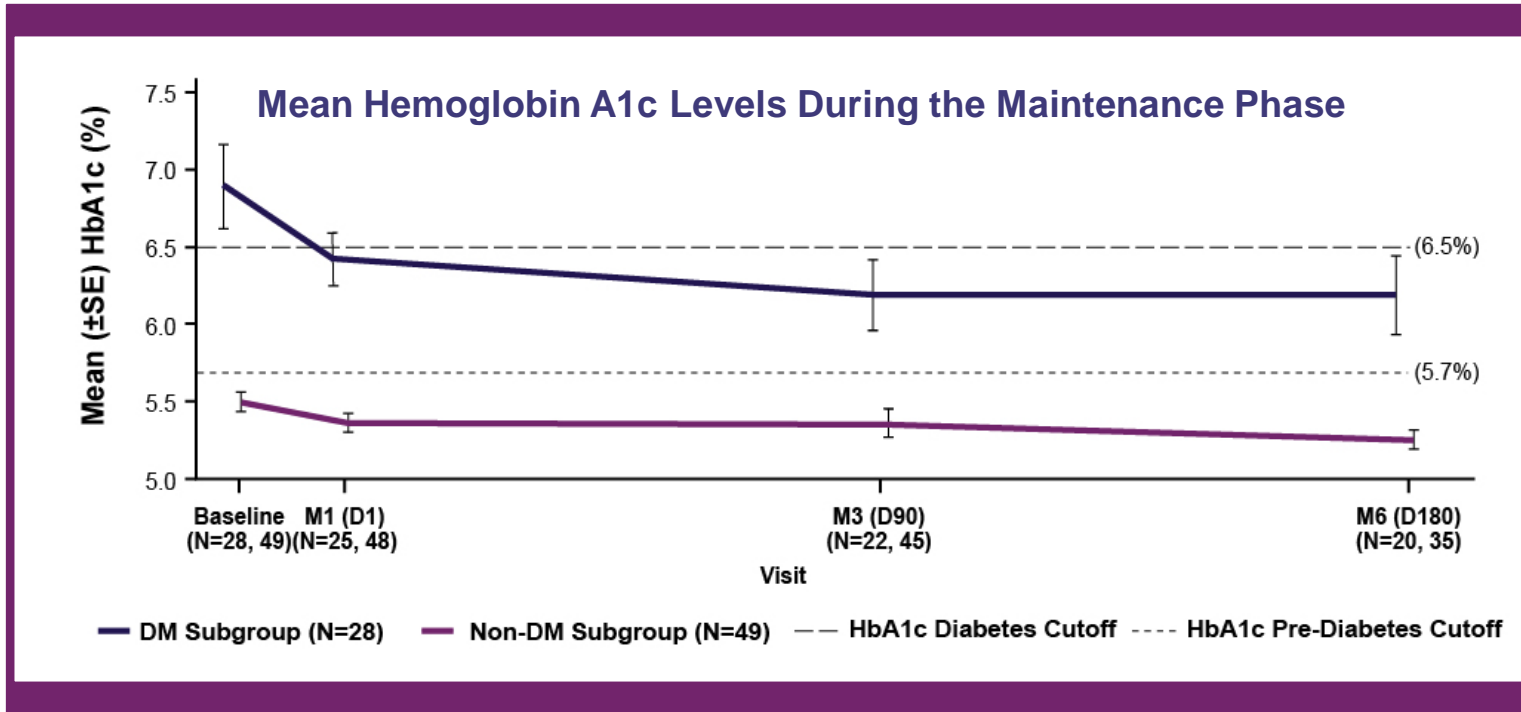
Extended evaluation phase (additional six months of maintenance therapy)

- 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)

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

Most commonly reported adverse events

All Phases Combined

Treatment-emergent events with incidence $\geq 15\%$

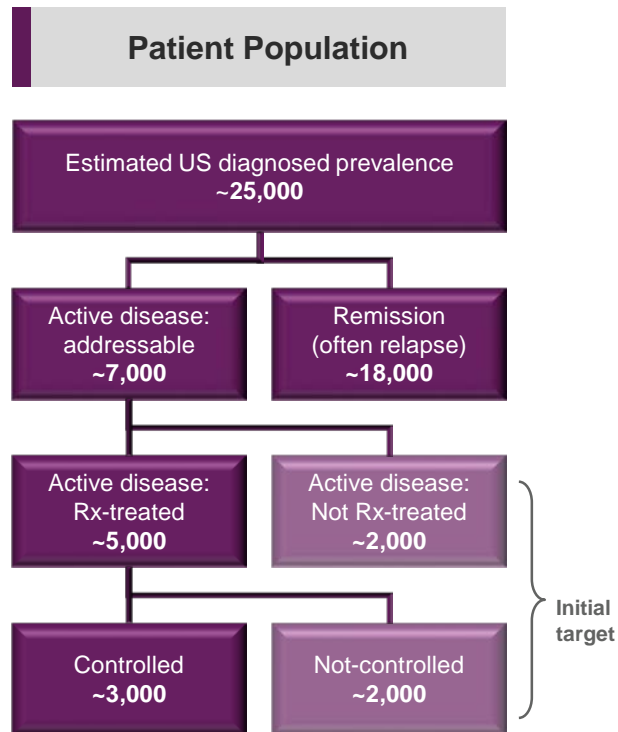
Adverse Event	% of enrolled (N=94)
Nausea	33%
Headache	29%
Peripheral edema	19%
Hypertension	19%
Fatigue	18%
ALT increased*	17%
Diarrhea	16%
Arthralgia	15%

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 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

- Regulatory update on NDA filing strategy (Q2 2019)
- Additional SONICS data to be reported at upcoming medical meetings
 - AACE – April 24-28, 2019
 - ECE – May 18-21, 2019
- LOGICS top-line data expected Q4 2019

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

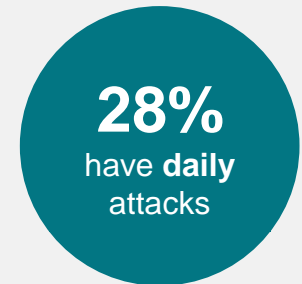
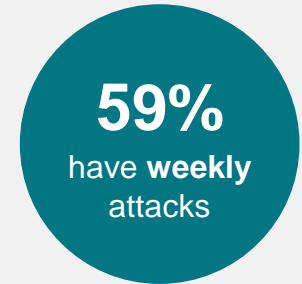
Impact of attacks

Paralytic attacks are acute episodes that can be debilitating⁴

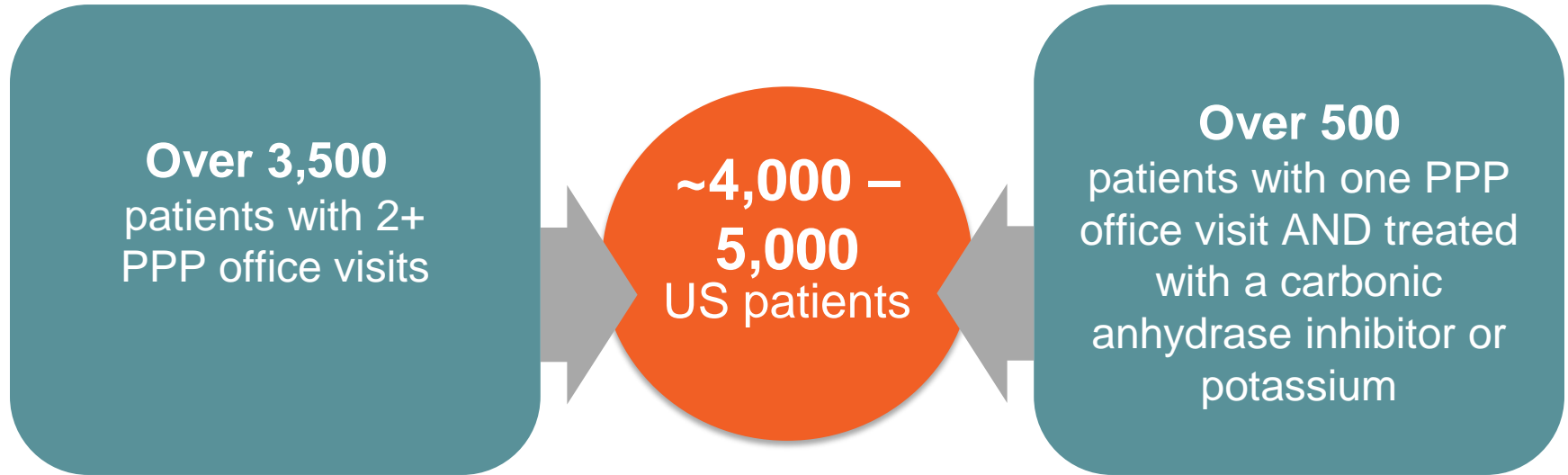
Attacks may last from one hour to several days¹

As patients age, muscle weakness can become permanent³

Frequency



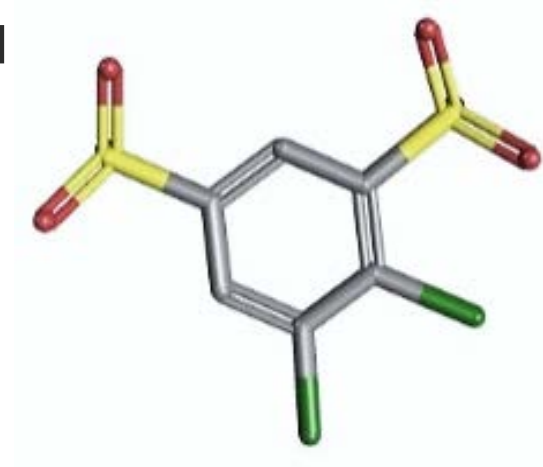
Estimated 4,000 – 5,000 diagnosed U.S. patients



* 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



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

2018 revenues: \$16.8M

2019 revenue guidance: \$18-20M

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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